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NEWS 19 Dec 19 CAS Roles modified
NEWS 20 Dec 19 1907-1946 data and page images added to CA and
CAplus
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E1 446 BJORCK L/AU
E2 7 BJORCK L H/AU

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              4 BJORCK LARS/AU
4 BJORCK LARS HENRIK/AU
1 BJORCK LENART/AU
15 BJORCK LENNART/AU
9 BJORCK LINNE A/AU
2 BJORCK LINNE A K/AU
4 BJORCK LINNE AGNETA/AU
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103 SJOBRING U/AU
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48 --> SJOBRING ULF/AU
1 SJOBROG S/AU
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1 SJODAHL CATHARINA/AU
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3 SJODAHL E J/AU
1 SJODAHL ERIC/AU
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 => s e2-e3
 L2 151 ("SJOBRING U"/AU OR "SJOBRING ULF"/AU)
 => s 11-12
 L3
              614 (L1 OR L2)
 => s 13 and immunoglobulin?
 L4
     233 L3 AND IMMUNOGLOBULIN?
 => s 14 and (protein 1 or light chain or hybrid)
     6 FILES SEARCHED...
                102 L4 AND (PROTEIN L OR LIGHT CHAIN OR HYBRID)
 => s 15 and domain?
 L6 62 L5 AND DOMAIN?
 => dup rem 16
 PROCESSING COMPLETED FOR L6
 L7 24 DUP REM L6 (38 DUPLICATES REMOVED)
 => d bib ab 1-24
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L7 ANSWER 1 OF 24 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD DUPLICATE

1

AN 2001-398077 [42] WPIDS

DNC C2001-121057

TI Novel vaccine composition comprising **protein L**, its analog or fragment, useful for enhancing immune response to an antigen in

an individual.

DC B04 D16

IN BJORCK, L; LEANDERSON, T; WICK, M J

PA (ACTI-N) ACTINOVA LTD

CYC 94

PI WO 2001043769 A2 20010621 (200142) * EN 25p

 ${\tt RW}\colon\thinspace {\tt AT}$ BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZW

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RU SD SE

SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW AU 2001021993 A 20010625 (200162)

ADT WO 2001043769 A2 WO 2000-GB4830 20001215; AU 2001021993 A AU 2001-21993

20001215

FDT AU 2001021993 A Based on WO 200143769

PRAI GB 1999-29937 19991217

AB WO 200143769 A UPAB: 20010726

NOVELTY - A vaccine composition (I) comprising **protein L** , its analog or fragment, coupled to a heterologous antigen, is new.

ACTIVITY - Immunosuppressive.

MECHANISM OF ACTION - Vaccine (claimed). Preparations of **Protein L** B1-B4, B1-B1 or B1 were incubated with

splenocytes from mice for 24, 48 or 72 hours in the presence or absence of

10 micro g/ml PMB. The level of surface expression of the co-stimulatory $% \left(1\right) =\left(1\right) \left(1\right) +\left(1\right) \left(1\right) \left(1\right) +\left(1\right) \left(1\right)$

molecules B7-1, B7-2 and CD40, as well as MHC-I and MHC-II expression on B $\,$

cells, was analyzed by fluorescence-activated cell sorting (FACS). The

result showed that protein L B1-B4 (5 micro g) as

well as B1-B1 (10 micro g) and B1 (10 micro g) caused up regulation of

B7-2 expression on gated B220+ cells, with the most dramatic effect

occurring with B1-B4. B1-B4 also upregulated CD40 and MHC-I expression,

but had no apparent effect on MHC-II. A slight influence of B1-B1 and B1

on surface expression of CD40 and MHC-I was detectable.

 $$\operatorname{USE}$ - (I) is useful for enhancing an immune response to an antigen in

```
Dwg.0/5
L7
    ANSWER 2 OF 24 USPATFULL
       2001:82536 USPATFULL
AN
       Treatment of bacterial infections
TI
      Bjorck, Lars, Lund, Sweden
ΙN
       Sjorbring, Ulf, Lund, Sweden
       Nasr, Abdelhakim Ben, Cambridge, United Kingdom
       Olsen, Arne, Bjarred, Sweden
       Herwald, Heiko, Malmo, Sweden
       Muller-Esterl, Werner, Mainz, Germany, Federal Republic of
       Mattsson, Eva, Lund, Sweden
       Actinova Limited, United Kingdom (non-U.S. corporation)
PΑ
PΙ
      US 6242210
                          B1
                               20010605
ΑI
      US 1999-258688
                               19990226 (9)
RLI
       Continuation of Ser. No. US 194098
DT
      Utility
FS
      Granted
EXNAM Primary Examiner: Leary, Louise N.
      Seed IP Law Group
CLMN
      Number of Claims: 5
ECL
       Exemplary Claim: 1
DRWN
       40 Drawing Figure(s); 18 Drawing Page(s)
LN.CNT 2437
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       An assay for compounds useful in the treatment of a bacterial
AΒ
induced
       coagulation disorder has the following steps:
       a) incubating a plasma sample with a strain of bacteria;
       b) adding a compound to be assayed to the plasma sample
before, during
      or after step (a);
       c) conducting an activated partial thromboplastin time test;
       d) determining the clotting time.
L7
     ANSWER 3 OF 24 USPATFULL
AN
       2001:59866 USPATFULL
       Use of kinin antagonists for preparing a pharmaceutical
TI
composition for
       treating bacterial infections
       Bjorck, Lars, Lund, Sweden
IN
       Sjobring, Ulf, Lund, Sweden
       Nasr, Abdelhakim Ben, Cambridge, United Kingdom
       Olsen, Arne, Lund, Sweden
       Herwald, Heiko, Lund, Sweden
       Muller-Esterl, Werner, Mainz, Germany, Federal Republic of
PA
       Actinova Limited, Cambridge, United Kingdom (non-U.S.
corporation)
PI
       US 6221845
                         B1
                               20010424
       WO 9744353 19971127
ΑI
       US 1999-194098
                             19990625 (9)
       WO 1997-SE825
                              19970520
                               19990625 PCT 371 date
```

an individual (claimed). Protein L is useful for

treating autoimmune diseases.

PRAI SE 1996-1901

DT Utility FS Granted

EXNAM Primary Examiner: Weddington, Kevin E.

LREP Seed IP Law Group PLLC

CLMN Number of Claims: 4

ECL Exemplary Claim: 1

DRWN 27 Drawing Figure(s); 13 Drawing Page(s)

LN.CNT 1607

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Kinin antagonists, especially bradykinin antagonists, can be used for

19960520

treating bacterial infections, in particular infections caused by

bacteria belonging to the genera Streptococcus, Escherichia, Salmonella,

Staphylococcus, Klebsiella, Moracella, Haemophilus and Yersinia.

L7 ANSWER 4 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 2

AN 2001220077 EMBASE

TI Immunoglobulin-binding domains of peptostreptococcal protein L enhance vaginal colonization of mice by Streptococcus gordonii.

AU Ricci S.; Medaglini D.; Marcotte H.; Olsen A.; Pozzi G.; Bjorck L.

CS S. Ricci, Department of Molecular Biology, Section for Microbiology,

University of Siena, 53100 Siena, Italy. riccisus@unisi.it

SO Microbial Pathogenesis, (2001) 30/4 (229-235).

Refs: 41

ISSN: 0882-4010 CODEN: MIPAEV

CY United Kingdom

DT Journal; Article

FS 004 Microbiology

005 General Pathology and Pathological Anatomy

LA English

SL English

AB Protein L, an immunoglobulin-binding protein

of some strains of the anaerobic bacterium $\ensuremath{\mathsf{Peptostreptococcus}}$ magnus, has

been hypothesized to be a virulence determinant in bacterial vaginosis. In

order to investigate the role of **protein L** in peptostreptococcal virulence, the Ig-binding **domains** of **protein L** were expressed at the surface of the human

oral commensal Streptococcus gordonii. Recombinant streptococci were used

in vaginal colonization experiments, and protein L

-expressing S. gordonii demonstrated enhanced ability to colonize the

vaginal mucosa. Compared to the control strain, they also persisted for a

longer period in the murine vagina. .COPYRGT. 2001 Academic Press.

L7 ANSWER 5 OF 24 USPATFULL

```
AN
       1999:124726 USPATFULL
TI
       Protein L and hybrid proteins thereof
       Bjorck, Lars, Sodra Sandby, Sweden
IN
       Sjobring, Ulf, Lund, Sweden
       Actinova Ltd., Lund, Sweden (non-U.S. corporation)
PA
PΙ
       US 5965390
                               19991012
                               19970211 (8)
ΑI
       US 1997-795475
RLI
       Division of Ser. No. US 1994-325278, filed on 26 Oct 1994
PRAI
       SE 1992-1331
                     19920428
DT
       Utility
FS
       Granted
EXNAM Primary Examiner: Degen, Nancy
LREP
       Seed and Berry LLP
CLMN
       Number of Claims: 11
ECL
       Exemplary Claim: 1
DRWN
       17 Drawing Figure(s); 17 Drawing Page(s)
LN.CNT 1305
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       The invention relates to sequences of protein L
       which bind to light chains of immunoglobulins. The invention
       also relates to hybrid proteins thereof which are able to bind
       to both light and heavy chains of immunoglobulin G, in
       particular protein LG. The invention also relates to
DNA-sequences which
       code for the proteins, vectors which include such
DNA-sequences, host
       cells which have been transformed with the vectors, methods for
       producing the proteins, reagent appliances for separation and
       identification of immunoglobulins, compositions and
       pharmaceutical compositions and pharmaceutical compositions
which
       contain the proteins.
     ANSWER 6 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI.
B.V.DUPLICATE 3
AN
     1998416862 EMBASE
     Protein LA, a novel hybrid protein with unique single-chain Fv
TI
     antibody- and Fab-binding properties.
     Svensson H.G.; Hoogenboom H.R.; Sjobring U.
ΑU
CS
    U. Sjobring, Department of Medical Microbiology, Solvegatan 23,
S-22362
     Lund, Sweden. ulf.sjobring@mmb.lu.se
SO
    European Journal of Biochemistry, (1 Dec 1998) 258/2 (890-896).
    Refs: 44
    ISSN: 0014-2956 CODEN: EJBCAI
CY
    United Kingdom
DT
    Journal; Article
FS
    026
             Immunology, Serology and Transplantation
             Clinical Biochemistry
    029
LΑ
    English
\operatorname{SL}
    English
AΒ
    Existing Ig-binding proteins all suffer from limitations in
their binding
     spectrum. In the pursuit of the ultimate, non-restricted,
Ig-binding
    protein, we have constructed the hybrid protein LA, by fusing
    four of the Ig.kappa. light-chain-binding
    domains of peptostreptococcal protein L with
    four of the IgGFc- and Fab-binding regions of staphylococcal
protein A.
```

Ligand-blot experiments demonstrated that the L and the A components were

both functional in the hybrid, as the protein was shown to bind purified x light chains and IgGFc. Protein LA bound human Ig of different

classes and IgG from a wide range of mammalian species. IgG, IgM and IqA $\,$

were purified from human serum and saliva by affinity chromatography on

protein LA agarose. Similarly, single-chain Fv (scFv) antibodies carrying

the .kappa. light-chain variable domain or

expressing the V(H)III (variable domain of the heavy chain of Ig) determinant, were efficiently purified on immobilized protein LA. As

judged by surface plasmon resonance (SPR), protein LA showed enhanced

affinity for all tested ligands, including several scFv antibodies,

compared with proteins ${\tt L}$ and ${\tt A}$ alone. SPR analysis also demonstrated that

binding of a ligand to one of the components in protein LA did not affect $\,$

the ability of the **hybrid** protein to interact simultaneously with a ligand for the other component. The antigen-binding capacity of a

.kappa.-expressing scFv antibody was unaffected by the interaction with

protein LA, whereas the binding of a V(H) III-expressing scFv antibody to

its antigen was, unexpectedly, blocked by protein A and protein LA.

Together, these data demonstrate that protein LA represents a highly

versatile Ig-binding molecule.

L7 ANSWER 7 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 4

AN 97086135 EMBASE

DN 1997086135

TI Solution structure of the albumin-binding GA module: A versatile bacterial

protein domain.

AU Johansson M.U.; De Chateau M.; Wikstrom M.; Forsen S.; Drakenberg T.;

Bjorck L.

CS M.U. Johansson, Department of Physical Chemistry 2, Chemical Center Lund

University, POB 124, S-221 00 Lund, Sweden

SO Journal of Molecular Biology, (1997) 266/5 (859-865).

Refs: 40

ISSN: 0022-2836 CODEN: JMOBAK

CY United Kingdom

DT Journal; Article

FS 029 Clinical Biochemistry

LA English

SL English

AB The albumin-binding GA module is found in a family of surface proteins of

different bacterial species. It comprises 45 amino acid residues and

represents the first known example of contemporary module shuffling. Using

1H NMR spectroscopy we have determined the solution structure of the ${\sf GA}$

module from protein PAB, a protein of the anaerobic human commensal and

pathogen Peptostreptococcus magnus. This structure, the first three-dimensional structure of an albumin-binding protein domain described, was shown to be composed of a left-handed three-helix-bundle.

Sequence differences between GA modules with different affinities for

albumin indicated that a conserved region in the C-terminal part of the

second helix and the flexible sequence between helices 2 and 3 could

contribute to the albumin-binding activity. The effect on backbone amide

proton exchange rates upon binding to albumin support this assumption. The

GA module has a fold that is strikingly similar to the immunoglobulin-binding domains of staphylococcal protein A but it shows no resemblance to the fold shared by the immunoglobulin-binding domains of streptococcal protein G and peptostreptococcal protein L. When the gene sequences, binding properties and thermal stability of these four domains are analysed in relation to their global folds an evolutionary pattern emerges. Thus, in the evolution of novel

properties mutations are allowed only as long as the energetically

favourable global fold is maintained.

L7 ANSWER 8 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 5

AN 97208477 EMBASE

DN 1997208477

TI NMR analysis of the interaction between **protein L** and Ig light chains.

AU Enokizono J.; Wikstrom W.; Sjobring U.; Bjorck L.; Forsen S.; Arata Y.; Kato K.; Shimada I.

CS W. Wikstrom, Department of Physical Chemistry 2, Lund University, Lund,

Sweden

SO Journal of Molecular Biology, (1997) 270/1 (8-13). Refs: 39

ISSN: 0022-2836 CODEN: JMOBAK

CY United Kingdom

DT Journal; Article

FS 004 Microbiology

O26 Immunology, Serology and Transplantation O29 Clinical Biochemistry

LA English

SL English

AB **Protein L** is a cell wall protein expressed by some strains of the anaerobic bacterial species Peptostreptococcus magnus. It

binds to immunoglobulin (Ig) light chains predominantly of the .kappa. subtype from a wide range of animal species. This binding is

mediated by five highly homologous repeats designated as B1-B5, each of

which comprises 72 to 76 amino acid residues. The fold of the Ig light chain-binding Bl domain of

protein L has previously been shown to comprise an

.alpha.-helix packed against a four-stranded .beta.-sheet. The Ig-binding

region of the protein L domain involves most

of the residues in the second .beta.-strand, the C-terminal residues of $\ensuremath{\mathsf{C}}$

the .alpha.-helix, and residues in the loop connecting the .alpha.-helix

with the third .beta.-strand. In the present study, we have identified the

protein L-binding site of an Ig light

chain by use of stable isotope-assisted NMR spectroscopy. The
light chain of a murine monoclonal anti-17.alpha.-

hydroxyprogesterone Fab fragment (IgG2b, .kappa.) was selectively labeled

with 13C at carbonyl groups of Ala, Arg, Cys, Ile, Lys, Met, Phe, Trp, or

Tyr. The residues in which the carbonyl 13C chemical shift was significantly perturbed upon binding of the **protein L**Bl **domain** were preferentially found in the second .beta.-strand of the variable .kappa. **domain** and parts of its flanking .beta.-strands. None of these residues were affected by the

the antigen against which the monoclonal Fab fragment is directed.

Therefore, we conclude that **protein L** binds to the outer surface of the framework region of the V(L) **domain**, primarily involving the V(L) second strand, and that this binding is

independent of antigen-binding. The present NMR data, in combination with

sequence comparisons between .kappa. light chains with and without

protein L affinity, suggest that the amino acid
 substitutions at positions 9, 20, and/or 74 of the .kappa. light
chains

could crucially affect the interaction between $protein\ L$ and the V(L) domain.

L7 ANSWER 9 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 6

addition of

AN 96327955 EMBASE

DN 1996327955

TI Protein PAB, an albumin-binding bacterial surface protein promoting growth

and virulence.

AU De Chateau M.; Holst E.; Bjorck L.

CS Department of Cell/Molecular Biology, Lund University, P.O. Box 94,S-221

00 Lund, Sweden

SO Journal of Biological Chemistry, (1996) 271/43 (26609-26615). ISSN: 0021-9258 CODEN: JBCHA3

```
CY United States
```

DT Journal; Article

FS 004 Microbiology

010 Obstetrics and Gynecology

026 Immunology, Serology and Transplantation

LA English

SL English

AB The anaerobic bacterium Peptostreptococcus magnus is a human commensal and

pathogen. Previous work has shown that strains of P. magnus isolated from

patients with gynecological disease (vaginosis) frequently express an

immunoglobulin (Ig) light chain-binding

protein called protein L. Here we report that strains

isolated from localized suppurative infections bind human serum albumin

(HSA), whereas commensal isolates bind neither Ig nor HSA. The HSA-binding

 $\,$ protein PAB was extracted from the bacterial surface or isolated from the

culture supernatant of the P. magnus strain ALBS. Protein PAB was shown to

have two homologous HSA-binding domains, GA and uGA. GA is absent in the sequence of a related protein from another P. magnus strain

and shows a high degree of homology to the HSA-binding domains of streptococcal protein G. Therefore GA is believed to have recently been

shuffled as a module from genes of other bacterial species into the

protein PAB gene. This GA module was shown to exhibit a much higher

affinity for HSA than uGA and was also found to be present in all of the

isolates tested from localized suppurative infections, indicating a role

in virulence. Moreover, when peptostreptococci or streptococci expressing

substantially increased. Thus, the \mbox{HSA} binding activity of the \mbox{GA} module

adds selective advantages to the bacteria, which increases their virulence

in the case of P. magnus strains.

L7 ANSWER 10 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 7

AN 96248384 EMBASE

DN 1996248384

TI Identification of interdomain sequences promoting the intronless evolution

of a bacterial protein family.

AU De Chateau M.; Bjorck L.

CS Section for Molecular Pathogenesis, Department of Cell/Molecular Biology,

Lund University, P.O. Box 94,S-221 00 Lund, Sweden

SO Proceedings of the National Academy of Sciences of the United States of

America, (1996) 93/16 (8490-8495). ISSN: 0027-8424 CODEN: PNASA6 CY United States DTJournal; Article FS 004 Microbiology LΑ English SL English In the evolution of eukaryotic genes, introns are believed to AΒ a major role in increasing the probability of favorable duplication events, chance recombinations, and exon shuffling resulting in functional hybrid proteins. As a rule, prokaryotic genes lack introns, and the examples of prokaryotic introns described do not seem to have contributed to gene evolution by exon shuffling. Still, certain families in modern bacteria evolve rapidly by recombination of duplication of functional domains, and as shown for protein PAB of the anaerobic bacterial species Peptostreptococcus magnus, by the shuffling of an albumin-binding protein module from group C and G streptococci. Characterization of a protein PAB- related gene in а Р. magnus strain with less albumin-binding activity revealed that the shuffled module was missing. Based on this fact and observations made when comparing gene sequences of this family of bacterial surface proteins interacting with albumin and/or immunoglobulin, a model is presented that can explain how this rapid intronless evolution takes place. A new kind of genetic element is introduced: the recer sequence promoting interdomain, in frame recombination and acting as a structureless flexibility-promoting spacer in the corresponding The data presented also suggest that antibiotics could represent the selective pressure behind the shuffling of protein modules in P. magnus, a member of the indigenous bacterial flora. ANSWER 11 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. L7B.V.DUPLICATE 8 ΑN 96295065 EMBASE DN1996295065 Characterization of the binding properties of protein LG, an TI immunoglobulin-binding hybrid protein. ΑU Kihlberg B.-M.; Sjoholm A.G.; Bjorck L.; Sjobring U. Department of Medical Microbiology, Lund University, S-223 62 CS Lund, Sweden SO European Journal of Biochemistry, (1996) 240/3 (556-563).

Immunology, Serology and Transplantation

ISSN: 0014-2956 CODEN: EJBCAI

CY

DT

FS

Germany

Journal; Article

029 Clinical Biochemistry

LA English

SL English

AB Protein LG is a 50-kDa hybrid molecule containing four Iglight-chain-binding domains from

protein L of Peptostreptococcus magnus and two IgG-Fc

binding repeats from streptococcal protein G. Here we analyse the binding

of protein LG to Ig from several mammalian species. Protein LG was shown

to bind human IgG of all subclasses and other Ig classes that carry $\ensuremath{\mathtt{K}}$

chains. The binding to human IgG was only marginally influenced by changes

in temperature (4-37.degree.C) or salt concentration $(0-1.6\ M)$, and was

stable over a wide pH range (pH 4-10). Protein LG bound to Ig from 11 of

12 mammalian species, including those of rabbit, mouse and rat. The

affinity constants obtained for the interactions between protein LG and

polyclonal IgG from rabbit (4.0 x 109 M-1), mouse (1.7 x 109 M-1) and rat

(1.3 X 109 M-1) were similar to the value previously reported for the $\,$

interaction between the **hybrid** protein and human polyclonal IgG (5.9 x 109M-1. The interaction between protein LG and a mouse IgG mAb was

not influenced by the presence of the specific protein antigen, nor was the

binding of this antibody to its ligand affected by protein LG. Inhibition

experiments demonstrated that the Ig-binding site of one of the fusion

partners retained its ligand-binding capacity when the other component was

occupied. Protein LG selectively absorbed 85-90% of the total Ig present

in human and rabbit sera and 75-80% of the Ig in sera from mouse and rat.

Human serum depleted of Clq, factor D and properdin and preabsorbed by

protein LG could be used as a source for other complement factors. These

data demonstrate that protein LG is a very versatile Ig-binding protein.

L7 ANSWER 12 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AN 95261390 EMBASE

DN 1995261390

TI Multiple ligand interactions for bacterial immunoglobulin -binding proteins on human and murine cells of the hematopoetic lineage.

AU Axcrona K.; Bjorck L.; Leanderson T.

CS The Immunology Unit, University of Lund, Solvegatan 21,S-223 62 Lund,

Sweden

SO Scandinavian Journal of Immunology, (1995) 42/3 (359-367).

ISSN: 0300-9475 CODEN: SJIMAX

CY United Kingdom

DT Journal; Article

FS 004 Microbiology

026 Immunology, Serology and Transplantation

029 Clinical Biochemistry

LA English

SL English

AB A group of bacterial Ig-binding surface proteins were studied: protein H

and M1 are from Streptococcus pyogenes and interact with IgG, protein L is expressed by Peptostreptococcus magnus and shows affinity for Ig light chains, whereas protein LG is a chimeric

construction combining the binding properties of **protein**L with the IgG-binding activity of protein G from group C and G streptococci. Proteins L and H coupled to Sepharose were mitogenic for

human peripheral blood lymphocytes (PBL) and mouse splenic B cells, but

not when added in soluble form. Differentiation to Ig secretion was

induced by protein H-Sepharose in mouse splenic B cells but not in human

PBLs. In FAGS analysis FITC-labelled protein H stained virtually all CD19+

cells in human peripheral blood as well as a majority of the CD3+ population. Protein L bound the majority of the CD19+

population, but also a fraction of the CD19-/CD3 population. Protein M1

was not mitogenic but stained the entire CD19+ population and 70% of the

CD3+ population. Identical staining patterns were observed with mouse

splenocytes using B220 and T-cell receptor as lineage markers. The $\,$

chimeric protein LG was a potent mitogen for mouse splenic B cells when

added either coupled to Sepharose or in soluble form. In addition, protein

LG induced differentiation to Ig secretion of the responding mouse splenic

B cells. In FAGS analysis, protein LG stained the entire CD19+

majority of the CD19-/CD3 lymphocyte population as well as all B220+ mouse

splenocytes and a fraction of the splenic T cells. These data indicate

that the bacterial proteins studied interact with surface structures of

several leucocyte populations and can hence interfere with the immune

system at multiple levels.

L7 ANSWER 13 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 9

AN 95224312 EMBASE

DN 1995224312

TI Mapping of the immunoglobulin light chain

```
-binding site of protein L.
     Wikstrom M.; Sjobring U.; Drakenberg T.; Forsen S.; Bjorck
ΑU
     Department of Physical Chemistry 2, Lund University, Lund, Sweden
CS
     Journal of Molecular Biology, (1995) 250/2 (128-133).
SO
     ISSN: 0022-2836 CODEN: JMOBAK
CY
     United Kingdom
DT
     Journal; Article
     004
             Microbiology
FS
             Immunology, Serology and Transplantation
     026
     029
             Clinical Biochemistry
     English
LΑ
     English
SL
AB
     Protein L is a cell surface protein expressed by some
     strains of the anaerobic bacterial species Peptostreptococcus
magnus. The
     molecule binds specifically and with high affinity to
     immunoglobulins (Ig) of a wide range of animal species. The
     Ig-binding activity is mediated through five highly homologous
     domains, each 72 to 76 amino acid residues long, which interact
     with framework regions in the variable domain of Iq light
     chains. The interaction does not interfere with the antiqen
binding
     capacity of the antibody. The fold of the Ig light chain
     -binding domains of Protein L is comprised
     of an .alpha.-helix packed against a four stranded .beta.-sheet
and is
     similar to the fold of the IqG heavy chain-binding domains of
     streptococcal protein G, despite the fact that the two proteins
show no
     significant sequence homology. In the present work,
heteronuclear NMR
     spectroscopy has been utilized to define the interaction between
the
     N-terminal Ig-binding domain of Protein L
     and the variable domain of a human Ig kappa light
     chain. The Ig-binding region of the Protein L
     domain involves most of the residues in the second .beta.-strand,
     the C-terminal residues of the .alpha.-helix and the loop
connecting the
     .alpha.-helix with the third .beta.-strand. The Ig light
     chain-binding surface of Protein L thus
     resembles the surface of Protein G which binds to the C.gamma.1
     domain of IqG, but is different from the portion of Protein G
     involved in the contact with the C.gamma.2-C.gamma.3 interface
region. The
     data suggest that the global fold shared by the Ig-binding
     of Proteins L and G provide bacteria with a flexible template
for the
     evolution of surface structures capable of interacting with
different
     conserved parts of Ig molecules of the infected host.
     ANSWER 14 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI.
B.V.DUPLICATE 10
AN
     95249085 EMBASE
DN
     1995249085
ΤI
     High level expression of protein L, an
```

```
immunoglobulin-binding protein, in Escherichia coli.
ΑU
     Tocaj A.; Sjobring U.; Bjorck L.; Holst O.
CS
     Dept. of Biotechnology, Chemical Center, Lund University, P.O.
Box
     124,S-221 00 Lund, Sweden
SO
     Journal of Fermentation and Bioengineering, (1995) 80/1 (1-5).
     ISSN: 0922-338X CODEN: JFBIEX
     Japan
CY
DT
     Journal; Article
FS
     027
             Biophysics, Bioengineering and Medical Instrumentation
     English
LA
SL
     English
     A high level expression system for production of an
AB
immunoglobulin
     - binding protein, in Escherichia coli was studied. The protein,
called
     protein L(I-IV), consists of four immunoglobulin
     -binding domains of the native protein L. A
     simple fed-batch cultivation strategy was used to investigate the
     influence of different induction times on cell growth,
viability, acetic
     acid formation and product formation. Induction allowing product
formation
     for several hours, i.e., in this case in early exponential
phase, was most
     favorable in terms of product yields. The highest specific yield
obtained
     was 150 mg protein per gram cell dry weight (dw), corresponding
to 360 mg
     per liter broth. The leakage of product into the media was less
than 5%.
     Induction in early exponential phase lead to the highest amount
of acetic
     acid, 1.47 g/g dw. Viability decreased significantly after
induction.
L7
     ANSWER 15 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI.
B.V.DUPLICATE 11
AN
     94380159 EMBASE
DN
     1994380159
TI
     Three-dimensional solution structure of an immunoglobulin
     light chain- binding domain of protein
     L. Comparison with the IgG-binding domains of protein G.
ΑU
     Wikstrom M.; Drakenberg T.; Forsen S.; Sjobring U.; Bjorck
CS
     Department of Physical Chemistry 2, Lund University, Lund, Sweden
SO
     Biochemistry, (1994) 33/47 (14011-14017).
     ISSN: 0006-2960 CODEN: BICHAW
CY
     United States
DT
     Journal; Article
FS
     029
             Clinical Biochemistry
LΑ
    English
SL
     English
AΒ
    Protein L is a multidomain protein expressed at the
     surface of some strains of the anaerobic bacterial species
     Peptostreptococcus magnus. It has affinity for immunoglobulin
     (Ig) through interaction with framework structures in the
     light chain domain. The Ig-binding activity is
```

located to five homologous repeats called B1-B5 in the N-terminal part of the protein. We have determined the three-dimensional solution structure of the 76 amino acid residue long B1 domain using NMR spectroscopy and distance geometry-restrained simulated annealing. The

domain is composed of a 15 amino acid residue long disordered

N-terminus followed by a folded portion comprising an

are well determined with a backbone atomic root mean square deviation from

their mean of 0.54 .ANG.. The B domains of protein

L show very limited sequence homology to the domains of streptococcal protein G interacting with the heavy chains of IqG. However,

despite this fact, and their different binding properties, the fold of the $\dot{}$

B1 domain was found to be similar to the fold of the IgG-binding protein G domains [Wikstrom, M., Sjobring, U., Kastern, W., Bjorck, L., Drakenberg, T., and Forsen, S. (1993) Biochemistry

3381-3386]. In the present study, the solution structure of the $\ensuremath{\mathtt{B1}}$

domain enabled a more detailed comparison which can explain the
 different Ig-binding specificities of these two bacterial surface
 proteins. Among the differences observed, the .alpha.-helix
 orientation is

the most striking. Thus, in the B1 domain of protein L the helix is almost parallel to the .beta.-sheet, whereas in the

protein G domains the helix runs diagonally across the sheet.

L7 ANSWER 16 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 12

32,

AN 94206234 EMBASE

DN 1994206234

TI Protein PAB, a mosaic albumin-binding bacterial protein representing the

first contemporary example of module shuffling.

AU De Chateau M.; Bjorck L.

CS Dept. of Medical/Physiological Chem., Lund University, P.O. Box 94,S-221

00 Lund, Sweden

SO Journal of Biological Chemistry, (1994) 269/16 (12147-12151). ISSN: 0021-9258 CODEN: JBCHA3

CY United States

DT Journal; Article

FS 004 Microbiology

LA English

SL English

AB Some strains of the anaerobic human commensal and pathogen Peptostreptococcus magnus bind human serum albumin (HSA), whereas other

strains of this species express protein L, an immunoglobulin light chain- binding surface

protein. A novel HSA-binding protein called protein PAB was purified in

one step from the culture supernatant of an HSA-binding strain of P.

magnus by affinity chromatography on HSA-Sepharose. The apparent size of

the molecule was 47 kDa on SDS-polyacrylamide gel electrophoresis. Amino

acid sequence analysis of protein PAB demonstrated that the $4\ \mathrm{NH2-terminal}$

residues were identical to the corresponding sequence in **protein** L. In a polymerase chain reaction, oligonucleotides based on extragenic 5'- and 3'- end sequences of the **protein** L

gene generated a product of the expected size: 1.3 kilobase pairs. A

recombinant protein with retained albumin binding capacity was expressed

in Escherichia coli, and the nucleotide sequence of the protein PAB gene

was determined. The structural gene is 1161 nucleotides long, corresponding to a preprotein of 387 amino acids and a molecular mass of

43,043 Da. Unlike most other Gram-positive bacterial surface proteins

described, protein PAB contains no internal homologies. However, substantial homologies were found to both proteins L and G (the IqG- and

HSA-binding surface protein of group C and G streptococci). The derived

amino acid sequence of the 135-base pair-long region homologous to protein

G corresponds to the HSA-binding domain of that protein, and in protein PAB, this region is inserted between sequences showing extensive

homology to COOH-terminal regions of peptostreptococcal **protein**L. This mosaic organization of protein PAB demonstrates that the
 molecule is a product of intergenic interspecies recombination
of a

functional **domain** into a common framework for peptostreptococcal surface proteins. Such an interspecies exchange of a functional protein

module has previously not been described in prokaryotic cells.

L7 ANSWER 17 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 13

AN 95022104 EMBASE

DN 1995022104

TI On the interaction between single chain Fv antibodies and bacterial

immunoglobulin-binding proteins.

AU Akerstrom B.; Nilson B.H.K.; Hoogenboom H.R.; Bjorck L.

CS Dept Medical/Physiological Chemistry, Lund University, P.O. Box 94,S-221

00 Lund, Sweden

SO Journal of Immunological Methods, (1994) 177/1-2 (151-163). ISSN: 0022-1759 CODEN: JIMMBG

CY Netherlands

DT Journal; Article

FS 004 Microbiology

026 Immunology, Serology and Transplantation

029 Clinical Biochemistry

```
LA English
SL English
AB Using four bacterial immunoglobulin-binding proteins, we have analyzed the binding characteristics of a panel of 34 human single chain
Fv antibodies, expressed in E. coli and with known specificity and sequence. Several of the single chain Fv antibodies showed affinity for staphylococcal protein A and peptostreptococcal protein
L, but not for the streptococcal proteins G or H. The affinity of the binding was higher for protein L (4.5 and 1.4 x
```

two single

containing

V(H)3

L7

AN

DN

ΤI

ΑU

CS

SO

CY

DT

LΑ

FS

EM

ED

AΒ

murine

blotting, and the

bacterial culture

non-binding V(L)

ANSWER 18 OF 24

Mariani M

English

199506

United States

Priority Journals

Entered STN: 19950615

Last Updated on STN: 19950615 Entered Medline: 19950602

95254583 MEDLINE

antibody fragments.

95254583 PubMed ID: 7736533

CELL BIOPHYSICS, (1994) 24-25 27-36.

Journal; Article; (JOURNAL ARTICLE)

Journal code: CQC; 8002185. ISSN: 0163-4992.

these

109 M-1) than for protein A (7.7 and 6.7 x 108 M-1), using the

A-Sepharose. Protein A, which has affinity for the V(H) domain of the scFv antibodies, was tested against scFv antibodies

V(L) **domain**, was tested against .kappa.1, .kappa.4, .lambda.1, .lambda.2 and .lambda.3 **domains**, and it bound all .kappa.1

domains demonstrated that amino acid residues crucial to the

Recombinant proteins L and LG. Two new tools for purification of

Biochemical Oncology Labs., SORIN Biomedica, Saluggia VC, Italy.

Vola R; Lombardi A; Tarditi L; Zaccolo M; Neri D; Bjorck L;

Several bacterial cell wall proteins, like proteins A and G,

affinity for immunoglobulins have been discovered and are

V(H)1, V(H)3, V(H)4 and V(H)5 domains, and its binding was restricted to approximately half of the scFv antibodies with a

ligands. The binding was shown to be specific by Western

single chain Fv antibodies could be purified from crude

media by affinity chromatography on protein L- or

domain. Protein L, which has affinity for the

domains, one .lambda.2 and one .lambda.3 domain.

Comparison of the amino acid sequences of binding and

binding of **protein L** were distributed over a large area outside the hypervariable antigen-binding regions.

MEDLINE

chain Fv antibodies displaying the strongest binding activity to

currently employed in immunological techniques. In 1988, protein L, a bacterial cell wall protein with Ig-binding capacity, was isolated from the anaerobic bacterial species Peptostreptococcus magnus.

Binding data with immunoglobulin fragments suggested that protein L could selectively bind the variable region of human kappa light chains. More recently a recombinant LG fusion protein

was expressed in E. coli containing four repeated Ig-binding domains of protein ${\bf L}$ (fragment B1-4) and two

IgG Fc-binding protein G domains (fragment CDC). Recombinant L and LG proteins were tested in the purification of murine monoclonal IgG

and their fragments. After affinity-constant evaluation in different

buffer systems, high-pressure affinity-chromatography columns were

prepared by coupling the proteins to Affi-prep 10 resin and tested with

eight different murine monoclonal antibodies and their fragments of

various isotypes. Affinity-chromatography experiments confirming radioimmunoassay results showed 75% fragment-binding capacity of protein L and 100% of protein LG. These results

evidenced protein LG as the most powerful Ig-binding tool so far described. Therefore, application of these proteins may be suggested in

the purification of murine immunoglobulins and their fragments, including the engineered ones.

L7 ANSWER 19 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 14

AN 93126906 EMBASE

DN 1993126906

TI Proton nuclear magnetic resonance sequential assignments and secondary

structure of an immunoglobulin light chain -binding domain of protein L.

AU Wikstrom M.; Sjobring U.; Kastern W.; Bjorck L.; Drakenberg T.; Forsen S.

CS Physical Chemistry 2, Chemical Center, P.O. Box 124,S-221 00 Lund, Sweden

SO Biochemistry, (1993) 32/13 (3381-3386).

ISSN: 0006-2960 CODEN: BICHAW

CY United States

DT Journal; Article

FS 004 Microbiology

026 Immunology, Serology and Transplantation

029 Clinical Biochemistry

LA English

SL English

AB The 1H NMR assignments have been made for the immunoglobulin (Ig) light chain-binding Bl domain of

 $protein\ L$ from Peptostreptococcus magnus. The secondary structure elements and the global folding pattern were determined from

nuclear Overhauser effects, backbone coupling constants, and slowly

exchanging amide protons. The B1 domain was found to be folded

into a globular unit of 61 amino acid residues, preceded by a 15 amino acid long disordered N-terminus. The folded portion of the molecule contains a four- stranded .beta.-sheet spanned by a central .alpha.-helix. The fold is similar to the IqG-binding domains of streptococcal protein G, despite the fact that the binding sites on immunoglobulin for the two proteins are different; protein G binds IgG through the constant (Fc) part of the heavy chain, whereas protein L has affinity for the variable domain of Ig light chains. L7ANSWER 20 OF 24 BIOSIS COPYRIGHT 2002 BIOSIS 1993:242227 BIOSIS ANDN PREV199344115427 NMR studies of an immunoglobulin light chain ΤI -binding protein L domain. Wikstrom, Mats (1); Sjobring, Ulf; Kastern, William; ΑU Bjorck, Lars; Drakenberg, Torbjorn; Forsen, Sture CS (1) Dep. Physical Chem., Univ. Lund, Lund Sweden Journal of Cellular Biochemistry Supplement, (1993) Vol. 0, No. SO 17 PART C, pp. 304. Meeting Info.: Keystone Symposium on Frontiers of NMR in Molecular Biology III Taos, New Mexico, USA March 8-14, 1993 ISSN: 0733-1959. DTConference LA English ANSWER 21 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. L7B.V.DUPLICATE 15 AN93269935 EMBASE DN1993269935 TI Purification of antibodies using protein L-binding framework structures in the light chain variable domain. ΑU Nilson B.H.K.; Logdberg L.; Kastern W.; Bjorck L.; Akerstrom B. Dept. of Medical/Physiol. Chemistry, University of Lund, P.O. CS Box 94,S-221 00 Lund, Sweden Journal of Immunological Methods, (1993) 164/1 (33-40). SO ISSN: 0022-1759 CODEN: JIMMBG CYNetherlands DTJournal; Article FS Microbiology Immunology, Serology and Transplantation 026 LΑ English SL English Protein L from the bacterial species AB Peptostreptococcus magnus binds specifically to the variable domain of Ig light chains, without interfering with the antigen-binding site. In this work a genetically engineered protein L, including four of the repeated Iq-binding repeat units, was employed for the purification of Ig from

various

sources. Thus, IgG, IgM, and IqA were purified from human and mouse serum in a single step using protein L-Sepharose affinity chromatography. Moreover, human and mouse monoclonal IgG, IgM, and human IgG Fab fragments, as well as a mouse/human chimeric recombinant antibody, could be purified from cultures of hybridoma cells or antibody-producing bacterial cells, with protein L -Sepharose. This was also the case with a humanized mouse antibody, in which mouse hypervariable antigen-binding regions had been introduced into a protein L-binding .kappa. subtype III human IgG. These experiments demonstrate that it is possible to engineer antibodies and antibody fragments (Fab, Fv) with protein L -binding framework regions, which can then be utilized in a protein L-based purification protocol. ANSWER 22 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. L7 B.V.DUPLICATE 16 AN 92243483 EMBASE DN1992243483 Structure of peptostreptococcal protein L and TIidentification of a repeated immunoglobulin light chain-binding domain. Kastern W.; Sjobring U.; Bjorck L. ΑU CS Department of Pathology, College of Medicine, University of Florida, Gainesville, FL 32610, United States SO Journal of Biological Chemistry, (1992) 267/18 (12820-12825). ISSN: 0021-9258 CODEN: JBCHA3 CY United States DTJournal; Article Microbiology FS 004 026 Immunology, Serology and Transplantation LA English SLEnglish The gene for protein L, an immunoglobulin AB (Ig) light chain-binding protein expressed by some strains of the anaerobic bacterial species Peptostreptococcus magnus, was cloned and sequenced. The gene translates into a protein of 719 amino acid residues. Following a signal sequence of 18 amino acids and a NH2-terminal region ('A') of 79 residues, the molecule contains five homologous 'B' repeats of 72-76 amino acids each. Further, toward the COOH terminus, two additional repeats ('C') were found. These are not related to the 'B'

repeats, but are highly homologous to each other. After the C repeats (52

amino acids each), a hydrophilic, proline-rich putative cell wall-spanning

region ('W') was found, followed at the COOH-terminal end by a hydrophobic

membrane anchor ('M'). Fragments of the gene were expressed, and the

corresponding peptides were analyzed for Ig-binding activity. The B repeats were found to be responsible for the interaction with Ig light chains. An Escherichia coli high level expression system was adapted for the production of large amounts of two Iq-binding protein L fragments comprising one and four B repeats, respectively. L7 ANSWER 23 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 17 AN 92311879 EMBASE DN 1992311879 TI Protein L from Peptostreptococcus magnus binds to the .kappa. light chain variable domain. ΑU Nilson B.H.K.; Solomon A.; Bjorck L.; Akerstrom B. Medical/Physiological Chem. Dept., University of Lund, P. O. Box CS 94,S-221 00 Lund, Sweden SO Journal of Biological Chemistry, (1992) 267/4 (2234-2239). ISSN: 0021-9258 CODEN: JBCHA3 CY United States DTJournal; Article FS 029 Clinical Biochemistry LΑ English SL English AB Protein L is an immunoglobulin light chain-binding protein expressed by some strains of the anaerobic bacterial species Peptostreptococcus magnus. The major variable region subgroups of human .kappa. and .lambda. light chains were tested for protein L binding; V(.kappa.I), V(.kappa.III), and V(.kappa.IV) bound protein L, whereas no binding occurred with proteins of the V(.kappa.II) subgroup or with any .lambda. light chain subgroups. Studies of the protein L binding capacity of naturally occurring V(L) fragments, and V(L) - and C(L) -related trypsin- and pepsin-derived peptides prepared from a .kappa.I light chain, localized the site of interaction to the V(L) domain. The affinity constant for the binding to an isolated V(.kappa.I) fragment was comparable to that for the native protein (K(.alpha.) 0.9 x 109 M-1 and K(.alpha.) 1.5 x respectively). No binding occurred with C(L)-related fragments. Extensive reduction and alkylation of the V(.kappa.) fragment or the native .kappa. chain resulted in complete loss of protein L binding. Although it is possible, from comparative amino acid sequence identify certain V(L)-framework region residues that account for the selective binding of protein L by .kappa.I, .kappa.III, and .kappa.IV proteins, our studies indicate that this interaction is essentially dependent upon the tertiary structural integrity of the .kappa. chain V(L) domain.

L7 ANSWER 24 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 18

AN 89281889 EMBASE

DN 1989281889

TI Ig-binding bacterial proteins also bind proteinase inhibitors.

AU Sjobring U.; Trojnar J.; Grubb A.; Akerstrom B.; Bjorck

CS Department of Medical Microbiology, University of Lund, 223 62 Lund,

Sweden

SO Journal of Immunology, (1989) 143/9 (2948-2954). ISSN: 0022-1767 CODEN: JOIMA3

CY United States

DT Journal

FS 004 Microbiology

026 Immunology, Serology and Transplantation

LA English

SL English

AB Protein G is a streptococcal cell wall protein with separate binding sites

for IgG and human serum albumin (HSA). In the present work it was demonstrated that .alpha.2-macroglobulin (.alpha.2M) and kininogen, two

proteinase inhibitors of human plasma, bound to protein G, whereas 23

other human proteins showed no affinity. .alpha.2M was found to interact

with the IgG-binding domains of protein G, and in excess .alpha.2M inhibited IgG binding and vice versa. A synthetic peptide,

corresponding to one of the homologous IgG-binding domains of protein G, blocked binding of protein G to .alpha.2M. Protein G showed

affinity for both native and proteinase complexed .alpha.2M but did not

bind to the reduced form of .alpha.2M, or to the C-terminal domain

of the protein known to interact with .alpha.2M receptors on macrophages.

Binding of protein ${\tt G}$ to .alpha.2M and kininogen did not interfere with

their inhibitory activity on proteinases, and the interaction between

 $\,$ protein G and the two proteinase inhibitors was not due to proteolytic

activity of protein G. The finding that protein G has affinity for

proteinase inhibitors was generalized to comprise also other Ig binding

bacterial proteins. Thus, .alpha.2M and kininogen, were shown to bind both

protein A of Staphylococcus aureus and **protein L** of Peptococcus magnus. The results described above suggest that Ig-binding

proteins are involved in proteolytic events, which adds a new and perhaps

functional aspect to these molecules.

```
=> s immunoglobulin? and (protein 1 or light chain or hybrid)
   6 FILES SEARCHED...
         39787 IMMUNOGLOBULIN? AND (PROTEIN L OR LIGHT CHAIN OR
L8
HYBRID)
=> s 18 and domain?
L9
          9085 L8 AND DOMAIN?
=> s 19 and immunoglobulin g
           850 L9 AND IMMUNOGLOBULIN G
L10
=> s 110 and protein l
            42 L10 AND PROTEIN L
L11
=> dup rem 111
PROCESSING COMPLETED FOR L11
L12
             31 DUP REM L11 (11 DUPLICATES REMOVED)
=> d bib ab 1-31
L12 ANSWER 1 OF 31 USPATFULL
AN
       2001:193946 USPATFULL
ΤI
       Enhancement of antibody-mediated immune responses
IN
       Ravetch, Jeffrey V., New York, NY, United States
PΙ
       US 2001036459
                         A1
                               20011101
       US 2001-834321
ΑI
                          A1
                               20010413 (9)
PRAI
      US 2000-198550
                          20000413 (60)
       US 2000-204254
                           20000515 (60)
       Utility
DT
FS
       APPLICATION
LREP
      Robin S, Quartin, Esq., Woodcock Washburn Kurtz, Mackiewicz &
Norris
       LLP, One Liberty Place-46th Floor, Philadelphia, PA, 19103
CLMN
      Number of Claims: 21
ECL
       Exemplary Claim: 1
DRWN
       3 Drawing Page(s)
LN.CNT 1679
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention is related to enhancing the function of
anti-tumor
       antibodies by regulating Fc.gamma.RIIB-mediated activity. In
particular,
       disrupting SHIP activation by Fc.gamma.RIIB enhances
cytotoxicity
       elicited by a therapeutic antibody in vivo in a human. The
invention
       further provides an antibody, e.g., an anti-tumor antibody,
with a
      variant Fc region that results in binding of the antibody to
      Fc.gamma.RIIB with reduced affinity. A variety of transgenic
```

mouse

models demonstrate that the inhibiting Fc.gamma.RIIB molecule is a potent regulator of cytotoxicity in vivo. L12 ANSWER 2 OF 31 USPATFULL 2001:36953 USPATFULL ΑN TICytokine signal regulators IN Yue, Henry, Sunnyvale, CA, United States Corley, Neil C., Mountain View, CA, United States Guegler, Karl J., Menlo Park, CA, United States Baughn, Mariah R., San Leandro, CA, United States Incyte Genomics, Inc., Palo Alto, CA, United States (U.S. PA corporation) PΙ US 6201106 B1 20010313 US 1999-382086 19990824 (9) ΑI Division of Ser. No. US 1998-189035, filed on 10 Nov 1998, now RLI patented, Pat. No. US 6020165, issued on 1 Feb 2000 DTUtility FS Granted EXNAM Primary Examiner: Prouty, Rebecca E.; Assistant Examiner: Monshipouri, Maryam LREP Incyte Genomics, Inc. CLMN Number of Claims: 4 ECLExemplary Claim: 1 15 Drawing Figure(s); 15 Drawing Page(s) DRWN LN.CNT 2393 CAS INDEXING IS AVAILABLE FOR THIS PATENT. The invention provides human cytokine signal regulators (CKSR) AΒ and polynucleotides which identify and encode CKSR. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for treating, or preventing disorders associated with expression of CKSR. L12 ANSWER 3 OF 31 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD AN2001-091926 [10] WPIDS DNC C2001-027208 Recombinant respiratory syncytial virus (RSV) incorporating a heterologous polynucleotide encoding an immune modulatory molecule is used as a vaccine to provide an immune response to RSV. DC B04 D16 BUKREYEV, A; COLLINS, P L; MURPHY, B R; WHITEHEAD, S S IN (USSH) US DEPT HEALTH & HUMAN SERVICES PA CYC 94 WO 2001004271 A2 20010118 (200110) * EN 154p RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC

RU SD SE

SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000062112 A 20010130 (200127)

ADT WO 2001004271 A2 WO 2000-US19042 20000712; AU 2000062112 A AU 2000-62112

20000712

FDT AU 2000062112 A Based on WO 200104271

PRAI US 1999-143425P 19990713

AB WO 200104271 A UPAB: 20010220

NOVELTY - Infectious recombinant respiratory syncytial virus (RSV) (I)

comprising a recombinant RSV genome or antigenome incorporating a heterologous polynucleotide encoding an immune modulatory molecule, a

major nucleocapsid (N) protein, nucleocapsid phosphoprotein (P),
large

polymerase **protein** (L) and a RNA polymerase elongation factor, is new.

 ${\tt DETAILED\ DESCRIPTION\ -\ INDEPENDENT\ CLAIMS\ are\ also\ included}$ for the

following:

(1) an isolated polynucleotide molecule (II) comprising a RSV genome

or antigenome modified to incorporate a polynucleotide sequence encoding

an immune modulatory molecule; and

(2) a method for producing an infectious attenuated RSV particle from

one or more isolated polynucleotide molecules encoding the RSV. ACTIVITY - Immunostimulator.

Balb/c mice were infected intranasally with 106 plaque forming units

(pfu) rRSV/mIFN gamma , rRSV/chloramphenicol acetyl transferase (CAT) or

wt RSV. Serum samples were collected on days 0, 28 and 56 and analyzed by $\,$

RSV-specific and antibody isotype-specific enzyme linked immunosorbent

assay and by an RSV neutralization assay. The levels of IgA antibodies

induced by the viruses were not significantly different, there was a

significant increase, four fold, in total IgG specific to RSV F protein in $% \left(1\right) =\left(1\right) +\left(1\right)$

mice vaccinated with rRSV/mIFN gamma compared to animals vaccinated with

wt RSV or RSV/CAT on day 56 but not on day 28. Neutralizing antibody

titers of mice infected with rRSV/mIFN gamma compared with wt RSV and

RSV/CAT were lower on day 28 but modestly higher on day 56.
MECHANISM OF ACTION - Vaccine.

 $$\operatorname{USE}$ - (I) elicits a protective immune response to RSV in a vaccinated

host (claimed). (I) is administered to an individual seronegative for

antibodies to RSV or possessing transplacentally acquired maternal

antibodies to RSV. (I) elicits an immune response against human RSV $\mbox{\sc A}$

and/or RSV B.

ADVANTAGE - (I) induces titers of serum Immunoglobulin ${\tt G}$ (IgG) that are at least 2-10 fold higher than levels of serum IgG induced by wt RSV.

Previously a chemotherapeutic agent ribavirin and pooled donor IgG

has been used to treat RSV but these methods lack long-term effectiveness

and are inappropriate for widespread use. Dwg.0/7

L12 ANSWER 4 OF 31 BIOSIS COPYRIGHT 2002 BIOSIS

AN 2001:261065 BIOSIS

DN PREV200100261065

TI Structures of the B1 domain of protein L

from Peptostreptococcus magnus with a tyrosine to tryptophan substitution.

AU O'Neill, Jason W.; Kim, David E.; Baker, David; Zhang, Kam Y. J. (1)

CS (1) Division of Basic Sciences, Fred Hutchinson Cancer Research Center,

1100 Fairview Avenue North, Seattle, WA, 98109: kzhang@fhcrc.org USA

SO Acta Crystallographica Section D Biological Crystallography, (April, 2001)

Vol. 57, No. 4, pp. 480-487. print.

ISSN: 0907-4449.

DT Article

LA English

SL English

AB The three-dimensional structure of a tryptophan-containing variant of the

IgG-binding B1 domain of protein L has been

solved in two crystal forms to 1.7 and 1.8 ANG resolution. In one of the

crystal forms, the entire N-terminal histidine-tag region was immobilized

through the coordination of zinc ions and its structural conformation

along with the zinc coordination scheme were determined. However, the

ordering of the histidine tag by zinc does not affect the overall structure of the rest of the protein. Structural comparisons of the

tryptophan-containing variant with an NMR-derived wild-type structure,

which contains a tyrosine at position 47, reveals a common fold, although

the overall backbone root-mean-square difference is 1.5 ANG. The Y47W

substitution only caused local rearrangement of several side chains, the

most prominent of which is the rotation of the Tyr34 side chain, resulting

in a 6 ANG displacement of its hydroxyl group. A small methyl-sized cavity

bounded by beta-strands 1, 2 and 4 and the alpha-helix was found in the

structures of the Y47W-substituted **protein L** B1 **domain**. This cavity may be created as the result of subsequent side-chain rearrangements caused by the Y47W substitution. These high-resolution structures of the tryptophan-containing variant provide a

reference frame for the analysis of thermodynamic and kinetic data derived

from a series of mutational studies of the $protein\ L$ B1 domain.

L12 ANSWER 5 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 1

AN 2001037308 EMBASE

TI Studies on a single immunoglobulin-binding domain of protein L from Peptostreptococcus magnus: The role of tyrosine-53 in the reaction with human IgG.

AU Beckingham J.A.; Housden N.G.; Muir N.M.; Bottomley S.P.; Gore M.G.

CS M.G. Gore, Div. of Biochemistry/Molecular Biol., School of Biological

Sciences, University of Southampton, Bassett Crescent East, Southampton,

Hants. S016 7PX, United Kingdom. m.g.gore@soton.ac.uk

SO Biochemical Journal, (15 Jan 2001) 353/2 (395-401).

Refs: 24

ISSN: 0264-6021 CODEN: BIJOAK

CY United Kingdom

DT Journal; Article

FS 004 Microbiology

LA English

SL English

AB Chemical modification experiments with tetranitromethane (TNM) have been

used to investigate the role of tyrosine residues in the formation of the

complex between PpL (the single Ig-binding domain of protein L, isolated from P. magnus strain 3316) and the kappa light chain (.kappa.-chain). Reaction of PpL with TNM causes the modification of 1.9 equiv. of tyrosine (Tyr(51) and

Tyr(53)) and results in an approx. 140-fold decrease in affinity for human

IgG. Similar experiments with mutated PpL proteins suggest that nitration

predominantly inactivates the protein by modification of Tyr(53).

Reduction of the nitrotyrosine groups to aminotyrosine by incubation with

sodium hydrosulphite does not restore high affinity for IgG. Modification

of .kappa.-chain by TNM resulted in the nitration of 3.1.+-.0.09 tyrosine

residues. When the PpL-.kappa.-chain complex was incubated with TNM,

4.1. + -.0.04 tyrosine residues were nitrated, indicating that one tyrosine

residue previously modified by the reagent was protected from $\ensuremath{\mathsf{TNM}}$ when the

proteins are in complex with each other. The K(d) for the equilibrium

between PpL, human IgG and their complex has been shown by ELISA to be 112

.+-. 20 nM. A similar value (153.+-.33nM) was obtained for the complex

formed between IgG and the Tyr(64) .fwdarw. Trp mutant (Y64W). However,

the K(d) values for the equilibria involving the PpL mutants Y53F and

Y53F,Y64W were found to be 3.2.+-.0.2 and 4.6.+-.1 .mu.M respectively.

These suggest that the phenol group of Tyr(53) in PpL is important to the

stability of the PpL-.kappa.-chain complex.

L12 ANSWER 6 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 2

AN 2001104980 EMBASE

TI A "loop entropy reduction" phage-display selection for folded amino acid

sequences.

AU Minard P.; Scalley-Kim M.; Watters A.; Baker D.

CS D. Baker, Department of Biochemistry, University or Washington, J 567

Health Sciences Building, Box 37-7350, Seattle, WA 98195, United States.

dabaker@u.washington.edu

SO Protein Science, (2001) 10/1 (129-134).

Refs: 25

ISSN: 0961-8368 CODEN: PRCIEI

CY United States

DT Journal; Article

FS 022 Human Genetics

029 Clinical Biochemistry

LA English

SL English

AB As a step toward selecting folded proteins from libraries of randomized

sequences, we have designed a 'loop entropy reduction'-based phage-display

method. The basic premise is that insertion of a long disordered sequence

into a loop of a host protein will substantially destabilize the host

because of the entropic cost of closing a loop in a disordered chain. If

the inserted sequence spontaneously folds into a stable structure with the

N and C termini close in space, however, this entropic cost is diminished.

The host protein function can, therefore, be used to select folded

inserted sequences without relying on specific properties of the inserted

sequence. This principle is tested using the IgG binding domain of protein L and the 1ck SH2 domain as host

proteins. The results indicate that the loop entropy reduction screen is

capable of discriminating folded from unfolded sequences when the proper

host protein and insertion point are chosen. L12 ANSWER 7 OF 31 BIOSIS COPYRIGHT 2002 BIOSIS AN 2001:243717 BIOSIS DNPREV200100243717 TI The role of tyrosine residues of protein L in the binding reaction with human IgG. AU Housden, N. G. (1); Beckingham, J. A. (1); Muir, N. M. (1); Bottomley, S. P. (1); Gore, M. G. (1) (1) Institute of Biomolecular Sciences, University of CS Southampton, Bassett Crescent East, Southampton, SO16 7PX UK Biochemical Society Transactions, (2001) Vol. 29, No. 1, pp. A22. print. Meeting Info.: 672nd Meeting of the Biochemical Society Sussex, England, UK ISSN: 0300-5127. DTConference LΑ English SL English L12 ANSWER 8 OF 31 USPATFULL AN2000:138515 USPATFULL ΤI Adsorbent for immunoglobulins and complexes thereof, adsorption method, and adsorption device IN Yasuda, Takamune, Kobe, Japan Odawara, Osamu, Takasago, Japan Ogino, Eiji, Kobe, Japan Nomura, Michio, Kakogawa, Japan Nakai, Takahisa, Kobe, Japan Asahi, Takashi, Kobe, Japan Tani, Nobutaka, Osaka, Japan PAKaneka Corporation, Osaka, Japan (non-U.S. corporation) PΙ US 6133431 20001017 WO 9726930 19970731 US 1998-117233 ΑI 19981020 (9) WO 1997-JP161 19970124 19981020 PCT 371 date 19981020 PCT 102(e) date PRAI JP 1996-11281 19960125 DTUtility FS Granted EXNAM Primary Examiner: Saunders, David LREP Fish & Neave, Haley, Jr., James F., Liang, Stanley D. CLMN Number of Claims: 20 ECL Exemplary Claim: 1 DRWN 7 Drawing Figure(s); 7 Drawing Page(s) LN.CNT 1489 CAS INDEXING IS AVAILABLE FOR THIS PATENT. An adsorbent that exhibits a high specificity in adsorbing immunoglobulins and/or complexes thereof, is extremely reduced in the lowering of the adsorption characteristic during

sterilization or storage, is highly stable and safe, and is prepared by

immobilizing on a

water-insoluble support either a peptide derivative which has undergone

at least one of the deletion, substitution, insertion, or addition of amino acids in a peptide having a specified amino acid sequence or an amino acid sequence, or the above peptide derivative which has the addition of Lyn or Cys at the amino and/or carboxyl terminal thereof; a device for adsorption and removal made by packing the adsorbent in a vessel equipped with effluent preventing means; and a method of adsorbing and removing immunoglobulins and/or complexes thereof contained in the blood, plasma or other body fluids with the adsorbent. L12 ANSWER 9 OF 31 USPATFULL 2000:80408 USPATFULL AN ΤI Compositions for the prevention and treatment of verotoxin-induced disease Williams, James A., Lincoln, NE, United States ΙN Byrne, Lisa Marie, Stoughton, WI, United States PA Ophidian Pharmaceuticals, Inc., Wisconsin, United States (U.S. corporation) US 6080400 PI20000627 ΑI US 1997-816977 19970313 (8) Continuation-in-part of Ser. No. US 1995-410058, filed on 24 RLI Mar 1995, now abandoned DT Utility FS Granted EXNAM Primary Examiner: Housel, James C.; Assistant Examiner: Devi, S. Medlen & Carroll, LLP LREP Number of Claims: 2 CLMN ECL Exemplary Claim: 1 1 Drawing Figure(s); 9 Drawing Page(s) DRWN LN.CNT 5468 CAS INDEXING IS AVAILABLE FOR THIS PATENT. AΒ The present invention includes methods for generating neutralizing antitoxin directed against verotoxins. In preferred embodiments, the antitoxin directed against these toxins is produced in avian species using soluble recombinant verotoxin proteins. This antitoxin is designed so as to be administrable in therapeutic amounts and may be in any form (i.e., as a solid or in aqueous solution). These antitoxins are useful in the treatment of humans and other animals intoxicated with one bacterial toxin, as well as for preventive treatment, and diagnostic assays to detect the presence of toxin in a sample.

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L12 ANSWER 10 OF 31 USPATFULL
ΑN
       2000:43944 USPATFULL
TI
       Purified and recombinant antigenic protein associated with
abdominal
       aortic aneurysm (AAA) disease, and diagnostic and therapeutic
use
       thereof
       Tilson, Martin David, Scarsdale, NY, United States
IN
       The Trustees of Columbia University, New York, NY, United
PA
States (U.S.
       corporation)
       US 6048704
PΙ
                               20000411
       US 1997-812586
ΑI
                               19970307 (8)
PRAI
       US 1996-12976
                           19960307 (60)
DT
       Utility
FS
       Granted
EXNAM Primary Examiner: Housel, James C.; Assistant Examiner:
Swartz, Rodney
       Ρ.
LREP
       White, John P. Cooper & Dunham LLP
CLMN
       Number of Claims: 9
       Exemplary Claim: 1
       22 Drawing Figure(s); 24 Drawing Page(s)
DRWN
LN.CNT 3522
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention provides an isolated protein of approximately
40 kDa
       which is purified from human aortic tissue and immunoreactive
with
       AAA-associated immunoglobulin. Also provided are a method of
       diagnosing AAA disease in a subject using said isolated
protein and a
       pharmaceutical composition comprising said isolated protein. A
method of
       alleviating AAA disease in a subject comprising administering
said
       pharmaceutical composition comprising the isolated protein is
also
       provided. The subject invention also provides a recombinantly
produced
       human aortic protein which is immunoreactive with
AAA-associated
     immunoglobulin. Also provided are a method of diagnosing AAA
       disease in a subject using said recombinantly produced protein
and a
       pharmaceutical composition comprising said recombinantly
produced
       protein. A method of alleviating AAA disease in a subject
comprising
       administering said pharmaceutical composition comprising the
       recombinantly produced protein is also provided.
L12 ANSWER 11 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI.
B.V.DUPLICATE 3
     2000328850 EMBASE
TI
    A breakdown of symmetry in the folding transition state of
protein
     Kim D.E.; Fisher C.; Baker D.
ΑU
```

D. Baker, Department of Biochemistry, University of Washington, Seattle, WA 98195, United States. dabaker@u.washington.edu SO Journal of Molecular Biology, (19 May 2000) 298/5 (971-984). Refs: 38 ISSN: 0022-2836 CODEN: JMOBAK CY United Kingdom DT Journal; Article FS Microbiology 004 Clinical Biochemistry 029 LΑ English SL English The 62 residue IgG binding domain of protein L ABconsists of a central .alpha.-helix packed on a four-stranded .beta.-sheet formed by N and C-terminal .beta.-hairpins. The overall topology of the protein is quite symmetric: The .beta.-hairpins have similar lengths and make very similar interactions with the central helix. Characterization of the effects of 70 point mutations distributed throughout the protein on the kinetics of folding and unfolding reveals that this symmetry is completely broken during folding; the first .beta.-hairpin is largely structured while the second .beta.-hairpin and helix are largely disrupted in the folding transition state ensemble. The results are not consistent with a 'hydrophobic core first' picture of protein folding; the first .beta.-hairpin appears to be at least as ordered at the rate limiting step in folding as the hydrophobic core. (C) 2000 Academic Press. L12 ANSWER 12 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V. AN2000290145 EMBASE TICritical role of .beta.-hairpin formation in protein G folding. ΑU McCallister E.L.; Alm E.; Baker D. CS D. Baker, Department of Biochemistry, University of Washington, Seattle, WA 98195, United States. dabaker@u.washington.edu SO Nature Structural Biology, (2000) 7/8 (669-673). ISSN: 1072-8368 CODEN: NSBIEW CY United States DT Journal; Article FS 029 Clinical Biochemistry LΑ English SLEnglish AB Comparison of the folding mechanisms of proteins with similar but very different sequences can provide fundamental insights into the determinants of protein folding mechanisms. Despite very little sequence similarity, the .apprx.60 residue IgG binding domains of protein

G and protein L both consist of a single helix packed

against a four-stranded sheet formed by two symmetrically disposed

.beta.-hairpins. We demonstrate that, as in the case of protein L, one of the two .beta.-turns of protein G is formed and the other disrupted in the folding transition state. Unlike protein L, however, in protein G it is the second .beta.-turn that is formed in the folding transition state ensemble. Substitution of

residue by Ala in protein G that eliminates an i,i+2 side chain-main chain

hydrogen bond in the second .beta.-turn slows the folding rate .apprx.20-fold but has virtually no effect on the unfolding

together with previous results, these findings suggest that the presence

of an intact .beta.-turn in the folding transition state is a

of the overall topology of protein L and protein G,

but the particular hairpin that is formed is determined by the

interatomic interactions that determine the free energies of formation of

the isolated .beta.-hairpins.

```
L12 ANSWER 13 OF 31 USPATFULL
AN
       1999:124726 USPATFULL
TI
       Protein L and hybrid proteins thereof
IN
       Bjorck, Lars, Sodra Sandby, Sweden
       Sjobring, Ulf, Lund, Sweden
PA
       Actinova Ltd., Lund, Sweden (non-U.S. corporation)
       US 5965390
                               19991012
PΙ
ΑI
      US 1997-795475
                               19970211 (8)
RLI
      Division of Ser. No. US 1994-325278, filed on 26 Oct 1994
PRAI
      SE 1992-1331
                          19920428
DT
      Utility
FS
      Granted
EXNAM Primary Examiner: Degen, Nancy
LREP
      Seed and Berry LLP
CLMN
      Number of Claims: 11
       Exemplary Claim: 1
ECL
DRWN
       17 Drawing Figure(s); 17 Drawing Page(s)
LN.CNT 1305
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The invention relates to sequences of protein L
```

AB

which bind to light chains of immunoglobulins. The invention also relates to hybrid proteins thereof which are able to bind to both light and heavy chains of immunoglobulin G,

in particular protein LG. The invention also relates to DNA-sequences

which code for the proteins, vectors which include such DNA-sequences,

host cells which have been transformed with the vectors, methods for

producing the proteins, reagent appliances for separation and identification of immunoglobulins, compositions and pharmaceutical compositions and pharmaceutical compositions

contain the proteins.

which

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L12
    ANSWER 14 OF 31 USPATFULL
       1999:18714 USPATFULL
AN
TI
       Gene therapy methods and compositions
IN
       Oin, Xiao-Oiang, Brighton, MA, United States
PA
       Biogen, Inc, Cambridge, MA, United States (U.S. corporation)
ΡI
       US 5869040
                               19990209
ΑI
       US 1995-481814
                               19950607 (8)
DT
       Utility
FS
       Granted
EXNAM Primary Examiner: Ketter, James; Assistant Examiner: Yucel,
Irem
LREP
       Biogen, Inc., Kaplan, Warren A.
CLMN
       Number of Claims: 23
ECL
       Exemplary Claim: 1
       2 Drawing Figure(s); 2 Drawing Page(s)
DRWN
LN.CNT 2515
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to uses of mutant
proto-oncogenes and
       oncoproteins expressed by the proto-oncogenes in inhibiting
tumor growth
       and/or inhibiting the transformed phenotype. The preferred
oncoprotein
       is a dominant, interfering mutant of a nuclear E2F
transcription factor
       protein and is preferably a mutant E2F1 transcription factor
protein.
       Methods of treating a target cell are described. Treatment is
       accomplished by administering to a target cell a dominant
interfering
       mutant of a proto-oncogene in an effective amount. Treatment
is also
       accomplished by administering to a target cell an oncoprotein
in an
       effective amount. Compositions for such use are described as
well.
L12 ANSWER 15 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN
     2000005317 EMBASE
TI
     Robustness of protein folding kinetics to surface hydrophobic
     substitutions.
     Gu H.; Doshi N.; Kim D.E.; Simons K.T.; Santiago J.V.; Nauli S.;
ΑU
Baker D.
    D. Baker, Department of Biochemistry, University of Washington,
Seattle,
     WA 98195, United States. dabaker@u.washington.edu
SO
     Protein Science, (1999) 8/12 (2734-2741).
     Refs: 21
     ISSN: 0961-8368 CODEN: PRCIEI
CY
    United States
DT
     Journal; Article
FS
    004
             Microbiology
LA
    English
SL
    English
    We use both combinatorial and site-directed mutagenesis to
explore the
     consequences of surface hydrophobic substitutions for the
folding of two
     small single domain proteins, the src SH3 domain, and
```

the IgG binding domain of Peptostreptococcal protein

L. We find that in almost every case, destabilizing surface hydrophobic substitutions have much larger effects on the rate of unfolding than on the rate of folding, suggesting that nonnative hydrophobic interactions do not significantly interfere with the rate of

core assembly.

L12 ANSWER 16 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AN 1999191641 EMBASE

TI Chain collapse can occur concomitantly with the rate-limiting step in

protein folding.

AU Plaxco K.W.; Millett I.S.; Segel D.J.; Doniach S.; Baker D.

CS D. Baker, Department of Biochemistry, University of Washington, Seattle,

WA 98195, United States. dabaker@u.washington.edu

SO Nature Structural Biology, (1999) 6/6 (554-556).

Refs: 26

ISSN: 1072-8368 CODEN: NSBIEW

CY United States

DT Journal; Article

FS 029 Clinical Biochemistry

LA English

SL English

of

AB We have directly characterized the extent of chain collapse early in the

folding of $protein\ L$ using time-resolved small angle X-ray scattering. We find that, immediately after the initiation

refolding, the protein exhibits dimensions indistinguishable from those

observed under highly denaturing, equilibrium conditions and that this

expanded initial state collapses with the same rate as that of the overall

folding reaction. The observation that chain compaction need not significantly precede the rate-limiting step of folding demonstrates that

rapid chain collapse is not an obligatory feature of protein folding

reactions.

L12 ANSWER 17 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 4

AN 1998388402 EMBASE

TI Limited internal friction in the rate-limiting step of a two-state protein

folding reaction.

AU Plaxco K.W.; Baker D.

CS D. Baker, Department of Biochemistry, Box 357350, University of Washington, Seattle, WA 98195-7350, United States. baker@ben.bchem.washington.edu

SO Proceedings of the National Academy of Sciences of the United States of

America, (10 Nov 1998) 95/23 (13591-13596).

Refs: 35

ISSN: 0027-8424 CODEN: PNASA6

CY United States

```
Journal; Article
DT
FS
            Clinical Biochemistry
LΑ
     English
     English
\operatorname{SL}
     Small, single-domain proteins typically fold via a compact
AΒ
     transition- state ensemble in a process well fitted by a simple,
two-state
     model. To characterize the rate-limiting conformational changes
that
     underlie two- state folding, we have investigated experimentally
the
     effects of changing solvent viscosity on the refolding of the
IqG binding
     domain of protein L. In conjunction with
     numerical simulations, our results indicate that the rate-
limiting
     conformational changes of the folding of this domain are
     strongly coupled to solvent viscosity and lack any significant
'internal
     friction' arising from intrachain collisions. When compared with
the
     previously determined solvent viscosity dependencies of other,
more
     restricted conformational changes, our results suggest that the
     rate-limiting folding transition involves conformational
fluctuations that
     displace considerable amounts of solvent. Reconciling evidence
that the
     folding transition state ensemble is comprised of highly
collapsed species
     with these and similar, previously reported results should
     significant constraint for theoretical models of the folding
process.
L12 ANSWER 18 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI.
B.V.DUPLICATE 5
ΑN
     1998416862 EMBASE
     Protein LA, a novel hybrid protein with unique single-chain Fv
ΤI
     antibody- and Fab-binding properties.
ΑU
     Svensson H.G.; Hoogenboom H.R.; Sjobring U.
CS
     U. Sjobring, Department of Medical Microbiology, Solvegatan 23,
S-22362
     Lund, Sweden. ulf.sjobring@mmb.lu.se
SO
     European Journal of Biochemistry, (1 Dec 1998) 258/2 (890-896).
     Refs: 44
     ISSN: 0014-2956 CODEN: EJBCAI
CY
     United Kingdom
DT
     Journal; Article
FS
     026
             Immunology, Serology and Transplantation
             Clinical Biochemistry
     029
LA
     English
SL
     English
     Existing Ig-binding proteins all suffer from limitations in
AΒ
their binding
     spectrum. In the pursuit of the ultimate, non-restricted,
Iq-binding
     protein, we have constructed the hybrid protein LA, by fusing
     four of the Ig.kappa. light-chain-binding
```

domains of peptostreptococcal protein L with
 four of the IgGFc- and Fab-binding regions of staphylococcal
protein A

Ligand-blot experiments demonstrated that the L and the A components were

both functional in the hybrid, as the protein was shown to bind purified x light chains and IgGFc. Protein LA bound human Ig of different

classes and IgG from a wide range of mammalian species. IgG, IgM and IgA $\,$

were purified from human serum and saliva by affinity chromatography on

protein LA agarose. Similarly, single-chain Fv (scFv) antibodies carrying

the .kappa. light-chain variable domain or

expressing the V(H)III (variable **domain** of the heavy chain of Ig) determinant, were efficiently purified on immobilized protein LA. As

judged by surface plasmon resonance (SPR), protein LA showed enhanced

affinity for all tested ligands, including several scFv antibodies,

compared with proteins ${\tt L}$ and ${\tt A}$ alone. SPR analysis also demonstrated that

binding of a ligand to one of the components in protein LA did not affect

the ability of the **hybrid** protein to interact simultaneously with a ligand for the other component. The antigen-binding capacity of a

.kappa.-expressing scFv antibody was unaffected by the interaction with

protein LA, whereas the binding of a V(H) III-expressing scFv antibody to

its antigen was, unexpectedly, blocked by protein A and protein ${\tt LA}\xspace$.

Together, these data demonstrate that protein LA represents a highly

versatile Ig-binding molecule.

L12 ANSWER 19 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 6

AN 97098945 EMBASE

DN 1997098945

TI Kinetics of folding of the IgG binding domain of peptostreptoccocal protein L.

AU Scalley M.L.; Yi Q.; Gu H.; McCormack A.; Yates III J.R.; Baker D.

CS D. Baker, Department of Biochemistry, University of Washington, Seattle,

WA 98195, United States

SO Biochemistry, (1997) 36/11 (3373-3382).

Refs: 38

ISSN: 0006-2960 CODEN: BICHAW

CY United States

DT Journal; Article

FS 029 Clinical Biochemistry

LA English

SL English

AB The kinetics of folding of a tryptophan containing mutant of the IgG

binding domain of protein L were

characterized using stopped-flow circular dichroism, stopped-flow fluorescence, and HD exchange coupled with high- resolution mass spectrometry. Both the thermodynamics and kinetics of folding fit well to

a simple two-state model: (1) Guanidine induced equilibrium denaturation

transitions measured by fluorescence and circular dichroism were virtually

superimposable. (2) The kinetics of folding/unfolding were single exponential under all conditions examined, and the rate constants obtained

using all probes were similar. (3) Mass spectra from pulsed HD exchange

refolding experiments showed that a species with very little protection

from exchange is converted to a fully protected species (the native state)

at a rate very similar to that of the overall change in tryptophan

fluorescence; no intervening partially protected species were observed.

(4) Rate constants (in H2O) and m values for folding and unfolding

determined by fitting observed relaxation rates obtained over a broad

range of denaturant concentrations to a two-state model were consistent

with the equilibrium parameters .DELTA.G and m: -RT

In(k(u)/k(f))/.DELTA.G(U)(H2O) = 1.02; (m(u) + m(f))/m = 1.08.In contrast

to results with a number of other proteins, there was no deviation from $\ \ \,$

linearity in plots of In k(obs) versus guanidine at low guanidine concentrations, both in the presence and absence of 0.4 M Na2SO4, suggesting that significantly stabilized intermediates do not accumulate

during folding. Although all of the change in fluorescence signal during $% \left(1\right) =\left(1\right) +\left(1\right) +\left$

folding in phosphate buffer was accounted for by the simple exponential

describing the overall folding reaction, fluorescence-quenching experiments using sodium iodide revealed a small reduction in the extent

of quenching of the protein within the first two milliseconds after $% \left(1\right) =\left(1\right) +\left(1\right)$

initiation of refolding in low concentrations of guanidine, suggesting a

partial collapse of the unfolded chain may occur under these conditions.

Comparison with results on the structurally and functionally similar IqG

binding domain of streptococcal protein G show intriguing differences in the folding of the two proteins.

L12 ANSWER 20 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 7

AN 96178843 EMBASE

DN 1996178843

TI Direct evidence for a two-state protein unfolding transition from hydrogen-deuterium exchange, mass spectrometry, and NMR.

AU Yi O.; Baker D.

CS Department of Biochemistry, University of Washington, Seattle, WA 98195,

United States

SO Protein Science, (1996) 5/6 (1060-1066). ISSN: 0961-8368 CODEN: PRCIEI

CY United States

DT Journal; Article

FS 029 Clinical Biochemistry

LA English

SL English

AB We use mass spectrometry in conjunction with hydrogen-deuterium exchange

and NMR to characterize the conformational dynamics of the 62-residue IgG

binding domain of protein L under conditions

in which the native state is marginally stable. Mass spectra of ${f protein}\ {f L}$ after short incubations in D2O reveal the

presence of two distinct populations containing different numbers of

protected protons. NMR experiments indicate that protons in the hydrophobic core are protected in one population, whereas all protons are

exchanged for deuterons in the other. As the exchange period is increased.

molecules are transferred from the former population to the latter. The

absence of molecules with a subset of the core protons protected suggests

that exchange occurs in part via a highly concerted transition to an

excited state in which all protons exchange rapidly with deuterons. A

steady increase in the molecular weight of the population with protected

protons, and variation in the exchange rates of the individual protected

protons indicates the presence of an additional exchange mechanism. $\ensuremath{\mathtt{A}}$

simple model in which exchange results from rapid (> 105/s) local fluctuations around the native state superimposed upon transitions to an

agreement between the observed mass spectra and the mass spectra simulated

according to the model using NMR-derived estimates of the proton exchange $% \left(1\right) =\left(1\right) +\left(1\right) +$

rates.

L12 ANSWER 21 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.DUPLICATE 8

AN 96295065 EMBASE

DN 1996295065

TI Characterization of the binding properties of protein LG, an immunoglobulin-binding hybrid protein.

AU Kihlberg B.-M.; Sjoholm A.G.; Bjorck L.; Sjobring U.

- CS Department of Medical Microbiology, Lund University, S-223 62 Lund, Sweden
- SO European Journal of Biochemistry, (1996) 240/3 (556-563). ISSN: 0014-2956 CODEN: EJBCAI
- CY Germany
- DT Journal; Article
- FS 026 Immunology, Serology and Transplantation 029 Clinical Biochemistry
- LA English
- SL English
- AB Protein LG is a 50-kDa hybrid molecule containing four Iglight-chain-binding domains from

protein L of Peptostreptococcus magnus and two IgG-Fc

binding repeats from streptococcal protein G. Here we analyse the binding

of protein LG to Ig from several mammalian species. Protein LG was shown

to bind human IgG of all subclasses and other Ig classes that carry K

chains. The binding to human IgG was only marginally influenced by changes

in temperature (4-37.degree.C) or salt concentration (0-1.6 M), ad was

stable over a wide pH range (pH 4-10). Protein LG bound to Ig from 11 of

12 mammalian species, including those of rabbit, mouse and rat. The

affinity constants obtained for the interactions between protein LG and

polyclonal IgG from rabbit (4.0 x 109 M-1), mouse (1.7 x 109 M-1) and rat

(1.3 X 109 M-1) were similar to the value previously reported for the $\,$

interaction between the hybrid protein and human polyclonal IgG (5.9 x 109M-1. The interaction between protein LG and a mouse IgG mAb was

not influenced by the presence of the specific protein antigen, nor was the

binding of this antibody to its ligand affected by protein LG.

experiments demonstrated that the Ig-binding site of one of the fusion

partners retained its ligand-binding capacity when the other component was

occupied. Protein LG selectively absorbed 85-90% of the total Ig present

in human and rabbit sera and 75-80% of the Ig in sera from mouse and rat.

Human serum depleted of Clq, factor D and properdin and preabsorbed by

protein LG could be used as a source for other complement factors. These

data demonstrate that protein LG is a very versatile Ig-binding protein.

- L12 ANSWER 22 OF 31 BIOSIS COPYRIGHT 2002 BIOSIS
- AN 1996:117934 BIOSIS
- DN PREV199698690069
- TI Backbone dynamics of a domain of protein L

which binds to immunoglobulin light chains.

AU Wikstrom, Mats (1); Forsen, Sture; Drakenberg, Torbjorn

CS (1) Physical Chem. 2, Chem. Cent., P.O. Box 121, S-221 00 Lund Sweden

SO European Journal of Biochemistry, (1996) Vol. 235, No. 3, pp. 543-548.

ISSN: 0014-2956.

DT Article

LA English

AB **Protein L** is a multidomain protein expressed at the surface of some strains of the anaerobic bacterial species Peptostreptococcus magnus. The molecule interacts with the variable

domain of immunoglobulin (1g) light chains through five repeated homologous domains denoted B1 to B5. The fold of the Ig-light-chain-binding B1 domain of

protein L (PLB1) has been shown to comprise an

alpha-helix packed against a four-stranded beta-sheet and therefore

resembles the structure of the IgG-binding domains of streptococcal protein G. In the present study, amide-proton exchange and

15N-relaxation NMR measurements were performed on the B1 domain to investigate its backbone mobility. It was shown that the folded portion

of PLB1 is rigid with no regions of significantly higher flexibility than

average. The N-terminus, however, is highly flexible consistent with

earlier studies on the solution structure of PLB1. Comparison of the

amide-proton-exchange data with similar measurements performed on the

IgG-binding domains of protein G indicates that the two proteins have different exchange behaviors in their second beta-strands.

protein G and L employ this region of their structures for binding to

immunoglobulins since the interaction of protein G and
protein L with IgG Fab and the Ig light
chain, respectively, involves residues from the second
beta-strand.

L12 ANSWER 23 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AN 95191451 EMBASE

DN 1995191451

TI A phage display system for studying the sequence determinants of protein

folding

AU Gu H.; Yi Q.; Bray S.T.; Riddle D.S.; Shiau A.K.; Baker D.

CS Department of Biochemistry, University of Washington, Seattle, WA 98195,

United States

SO Protein Science, (1995) 4/6 (1108-1117). ISSN: 0961-8368 CODEN: PRCIEI

CY United States

DT Journal; Article

FS 029 Clinical Biochemistry

LA English

SL English

AB We have developed a phage display system that provides a means to select

variants of the IgG binding domain of peptostreptococcal protein L that fold from large combinatorial libraries. The premise underlying the selection scheme is that binding of protein L to IgG requires that the protein be properly folded. Using a combination of molecular biological and biophysical

methods, we show that this assumption is valid. First, the phage selection

procedure strongly selects against a point mutation in **protein**L that disrupts folding but is not in the IgG binding interface.
Second, variants recovered from a library in which the first

protein L was randomized are properly folded. The degree
 of sequence variation in the selected population is striking:
the variants

have as many as nine substitutions in the 14 residues that were mutagenized. The approach provides a selection for 'foldedness' that is

potentially applicable to any small binding protein.

L12 ANSWER 24 OF 31 JICST-EPlus COPYRIGHT 2002 JST

AN 950744862 JICST-EPlus

TI High Level Expression of Protein L, an Immunoglobulin-Binding Protein, in Escherichia coli.

AU TOCAJ A; SJOEBRING U; BJOERCK L; HOLST O

CS Lund Univ., Lund, SWE

SO J Ferment Bioeng, (1995) vol. 80, no. 1, pp. 1-5. Journal Code: G0535B

(Fig. 2, Tbl. 1, Ref. 20)

CODEN: JFBIEX; ISSN: 0922-338X

CY Japan

DT Journal; Article

LA English

STA New

AB A high level expression system for production of an immunoglobulin

-binding protein, in Escherichia coli was studied. The protein, called

protein LI-IV, consists of four immunoglobulin-binding domains of the native protein L. A simple

fed-batch cultivation strategy was used to investigate the influence of

different induction times on cell growth, viability, acetic acid formation

and product formation. Induction allowing product formation for several

hours, i.e., in this case in early exponential phase, was most favorable

in terms of product yields. The highest specific yield obtained was $150\ \mathrm{mg}$

protein per gram cell dry weight (dw), corresponding to 360 mg per liter

broth. The leakage of product into the media was less than 5%. Induction

in early exponential phase lead to the highest amount of acetic acid, 1.47

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q/q dw. Viability decreased significantly after induction.
(author abst.)
L12 ANSWER 25 OF 31 BIOSIS COPYRIGHT 2002 BIOSIS
AN
    1995:68832 BIOSIS
DN
    PREV199598083132
    Three-dimensional solution structure of an immunoglobulin
TI
     light chain-binding domain of protein
     L. comparison with the IqG-binding domains of protein G.
    Wikstrom, Mats (1); Drakenberg, Torbjorn; Forsen, Sture;
ΑU
Sjobring, Ulf;
     Bjorck, Lars
     (1) Dep. Physical Chem. 2, Medical Microbiol., Lund University,
CS
Lund
     Biochemistry, (1994) Vol. 33, No. 47, pp. 14011-14017.
SO
     ISSN: 0006-2960.
DT
    Article
    English
LΑ
    Protein L is a multidomain protein expressed at the
AΒ
     surface of some strains of the anaerobic bacterial species
     Peptostreptococcus magnus. It has affinity for immunoglobulin
     (Ig) through interaction with framework structures in the
variable Iq
     light chain domain. The Ig-binding activity is
     located to five homologous repeats called B1-B5 in the
N-terminal part of
     the protein. We have determined the three-dimensional solution
structure
     of the 76 amino acid residue long B1 domain using NMR
     spectroscopy and distance geometry-restrained simulated
annealing. The
     domain is composed of a 15 amino acid residue long disordered
     N-terminus followed by a folded portion comprising an
alpha-helix packed
     against a four-stranded beta-sheet. These secondary structural
elements
     are well determined with a backbone atomic root mean square
deviation from
     their mean of 0.54 ANG . The B domains of protein
     L show very limited sequence homology to the domains of
     streptococcal protein G interacting with the heavy chains of
IgG. However,
     despite this fact, and their different binding properties, the
fold of the
     B1 domain was found to be similar to the fold of the IgG-binding
     protein G domains (Wikstrom, M., Sjobring, U., Kastem, W.,
     Bjorck, L., Drakenberg, T., & Forsen, S. (1993) Biochemistry 32,
     3381-3386). In the present study, the solution structure of the
B1
     domain enabled a more detailed comparison which can explain the
     different Iq-binding specificities of these two bacterial surface
     proteins. Among the differences observed, the alpha-helix
orientation is
     the most striking. Thus, in the B1 domain of protein
     L the helix is almost parallel to the beta-sheet, whereas in the
     protein G domains the helix runs diagonally across the sheet.
```

L12 ANSWER 26 OF 31 BIOSIS COPYRIGHT 2002 BIOSIS

```
1994:346388 BIOSIS
AN
DN
     PREV199497359388
TI
     Immunoglobulin Fab fragment-binding proteins.
     Bouvet, Jean-Pierre
ΑU
     Unite d'Immunologie Microbienne, Inst. Pasteur, 25 rue Dr Roux,
CS
F-75724
     Paris 15 France
     International Journal of Immunopharmacology, (1994) Vol. 16, No.
SO
5-6, pp.
     419-424.
     ISSN: 0192-0561.
DT
     General Review
LA
     English
AB
     Five molecules are known to bind the Fab fragments of human
     immunoglobulins (Iq). Microbial protein A and protein G are
     primarily Fc-binding molecules but can also bind other
structures of the
     heavy chain, which are located in the variable domain of the
     third subgroup (V-H3) and in the first constant domain of IgG
     (C-H1-r), respectively. In contrast, the two other microbial
receptors
     have a sole Iq-binding site, directed to kappa chains (protein
     L) or to Ig polymers (protein P). Protein Fv is synthesized by
     human liver cells and released in the digestive lumen, where it
forms
     large complexes with secretory Iq after binding to the VH domains
     . These five molecules, in the main, bind cleaved Ig and most of
     recognize all classes of antibodies. Bacterial molecules are, or
can be,
     used as reagents to purify and detect Ig and fragments.
Furthermore, a
     possible use in human therapy or vaccination is envisaged, and
the human
     protein Fv is a key-factor in immune protection against
intraluminal
     pathogens of the gut.
L12 ANSWER 27 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN
     93126906 EMBASE
DN
     1993126906
TI
     Proton nuclear magnetic resonance sequential assignments and
secondary
     structure of an immunoglobulin light chain
     -binding domain of protein L.
ΑU
     Wikstrom M.; Sjobring U.; Kastern W.; Bjorck L.; Drakenberg T.;
Forsen S.
CS
     Physical Chemistry 2, Chemical Center, P.O. Box 124,S-221 00
Lund, Sweden
     Biochemistry, (1993) 32/13 (3381-3386).
     ISSN: 0006-2960 CODEN: BICHAW
CY
     United States
DT
     Journal; Article
FS
     004
             Microbiology
             Immunology, Serology and Transplantation
     026
     029
             Clinical Biochemistry
     English
LΑ
\operatorname{SL}
     English
AΒ
     The 1H NMR assignments have been made for the immunoglobulin
```

(Iq) light chain-binding B1 domain of protein L from Peptostreptococcus magnus. The secondary structure elements and the global folding pattern were determined from nuclear Overhauser effects, backbone coupling constants, and slowly exchanging amide protons. The B1 domain was found to be folded into a globular unit of 61 amino acid residues, preceded by a 15 acid long disordered N-terminus. The folded portion of the molecule contains a four- stranded .beta.-sheet spanned by a central .alpha.-helix. The fold is similar to the IgG-binding domains of streptococcal protein G, despite the fact that the binding sites on immunoglobulin for the two proteins are different; protein G binds IgG through the constant (Fc) part of the heavy chain, whereas protein L has affinity for the variable domain of Ig light chains. L12 ANSWER 28 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 9 AN 93269935 EMBASE DN 1993269935 ΤI Purification of antibodies using protein L-binding framework structures in the light chain variable Nilson B.H.K.; Logdberg L.; Kastern W.; Bjorck L.; Akerstrom B. AU Dept. of Medical/Physiol. Chemistry, University of Lund, P.O. CS Box 94, S-221 00 Lund, Sweden SO Journal of Immunological Methods, (1993) 164/1 (33-40). ISSN: 0022-1759 CODEN: JIMMBG CY Netherlands DT Journal; Article FS Microbiology 004 026 Immunology, Serology and Transplantation LAEnglish SLEnglish AΒ Protein L from the bacterial species Peptostreptococcus magnus binds specifically to the variable domain of Ig light chains, without interfering with the antigen-binding site. In this work a genetically engineered fragment of protein L, including four of the repeated Ig-binding repeat units, was employed for the purification of Ig from sources. Thus, IgG, IgM, and IgA were purified from human and mouse serum in a single step using protein L-Sepharose affinity chromatography. Moreover, human and mouse monoclonal IgG, IgM, and IgA,

and human IgG Fab fragments, as well as a mouse/human chimeric recombinant

antibody, could be purified from cultures of hybridoma cells or antibody-producing bacterial cells, with protein L

-Sepharose. This was also the case with a humanized mouse antibody, in

which mouse hypervariable antigen-binding regions had been introduced into

a protein L-binding .kappa. subtype III human IgG.

These experiments demonstrate that it is possible to engineer antibodies

and antibody fragments (Fab, Fv) with **protein L** -binding framework regions, which can then be utilized in a **protein L**-based purification protocol.

L12 ANSWER 29 OF 31 BIOSIS COPYRIGHT 2002 BIOSIS

AN 1991:342266 BIOSIS

DN BA92:41641

TI EFFICIENT EXPRESSION OF A TRYPANOSOMA-CRUZI ANTIGEN IN ESCHERICHIA-COLI

AND STAPHYLOCOCCUS-AUREUS AND ITS RAPID PURIFICATION.

AU MORENO J I; SEIGELCHIFER M; ZORZOPULOS J

CS DEP. MOL. GENETICS, BIOSIDUS S.A., CONSTITUCION 4234, 1254 BUENOS AIRES,

ARGENTINA.

SO WORLD J MICROBIOL BIOTECHNOL, (1991) 7 (3), 316-323. CODEN: WJMBEY. ISSN: 0959-3993.

FS BA: OLD

LA English

AB A Trypanosoma cruzi antigen gene was closed into a fusion vector based on

the IgG binding **domain** of Staphylococcus aureus protein A. This vector transformed into Escherichia coli or Staphylococcus aureus and

produced about 12 mg fusion protein/l culture. In E.

coli, the product remained intracellular while in S. aureus it was

excreted into the growth medium. The **hybrid** protein was purified by IgG Sepharose affinity chromatography. The presence of a cleavage site

for enterokinase between protein A and the T. cruzi antigen in the fusion

protein allowed the efficient release of the unfused antigen by enzymatic

treatment. Further affinity chromatography through IgG Sepharose resulted

in the production of the T. cruzi antigen free of protein A.

L12 ANSWER 30 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AN 89281889 EMBASE

DN 1989281889

TI Ig-binding bacterial proteins also bind proteinase inhibitors.

AU Sjobring U.; Trojnar J.; Grubb A.; Akerstrom B.; Bjorck L.

CS Department of Medical Microbiology, University of Lund, 223 62 Lund,

Sweden

SO Journal of Immunology, (1989) 143/9 (2948-2954). ISSN: 0022-1767 CODEN: JOIMA3

CY United States

DT Journal

FS 004 Microbiology

026 Immunology, Serology and Transplantation

LA English

SL English

AB Protein G is a streptococcal cell wall protein with separate binding sites

for IgG and human serum albumin (HSA). In the present work it was demonstrated that .alpha.2-macroglobulin (.alpha.2M) and kininogen, two

proteinase inhibitors of human plasma, bound to protein G, whereas 23

other human proteins showed no affinity. .alpha.2M was found to interact

with the IgG-binding domains of protein G, and in excess .alpha.2M inhibited IgG binding and vice versa. A synthetic peptide,

corresponding to one of the homologous IgG-binding domains of protein G, blocked binding of protein G to .alpha.2M. Protein G showed

affinity for both native and proteinase complexed .alpha.2M but did not

bind to the reduced form of .alpha.2M, or to the C-terminal domain

of the protein known to interact with .alpha.2M receptors on macrophages.

Binding of protein G to .alpha.2M and kininogen did not interfere with

their inhibitory activity on proteinases, and the interaction between

protein ${\tt G}$ and the two proteinase inhibitors was not due to proteolytic

activity of protein G. The finding that protein G has affinity for

proteinase inhibitors was generalized to comprise also other Ig binding

bacterial proteins. Thus, .alpha.2M and kininogen, were shown to bind both

protein A of Staphylococcus aureus and protein L of

Peptococcus magnus. The results described above suggest that Ig-binding

proteins are involved in proteolytic events, which adds a new and perhaps

functional aspect to these molecules.

- L12 ANSWER 31 OF 31 LIFESCI COPYRIGHT 2002 CSA
- AN 89:66455 LIFESCI
- TI Ig-binding bacterial proteins also bind proteinase inhibitors.
- AU Sjoebring, U.; Trojnar, J.; Grubb, A.; Aakerstroem, B.; Bjoerck, L.
- CS Dep. Med. Microbiol., Soelvegatan 23, S-223 62 Lund, Sweden
- SO J. IMMUNOL., (1989) vol. 143, no. 9, pp. 2948-2954.
- DT Journal
- FS J; F
- LA English
- SL English
- AB Protein G is a streptococcal cell wall protein with separate binding sites

for IgG and human serum albumin (HSA). In the present work it was demonstrated that alpha sub(2)-macroglobulin (alpha sub(2)M) and

kininogen, two proteinase inhibitors of human plasma, bound to protein G,

whereas 23 other human proteins showed no affinity. alpha sub(2)M was

found to interact with the IgG-binding domains of protein G, and

in excess alpha sub(2)M inhibited IgG binding and vice versa. alpha

 $\operatorname{sub}(2)M$ and kininogen were shown to bind both protein A of Staphylococcus

aureus) and protein L of Peptococcus magnus . The

results described above suggest that Ig-binding proteins are involved in

proteolytic events, which adds a new and perhaps functional aspect to

these molecules.

=> d his

(FILE 'HOME' ENTERED AT 15:58:56 ON 18 JAN 2002)

FILE 'EMBASE, MEDLINE, BIOSIS, USPATFULL, JAPIO, WPIDS, CAPLUS, AGRICOLA,

LIFESCI, BIOTECHDS, JICST-EPLUS' ENTERED AT 15:59:04 ON 18 JAN 2002

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E BJORCK LARS/AU
L1
            532 S E1-E4
                E SJOBRING ULF/AU
L2
            151 S E2-E3
L3
            614 S L1-L2
L4
            233 S L3 AND IMMUNOGLOBULIN?
L5
            102 S L4 AND (PROTEIN L OR LIGHT CHAIN OR HYBRID)
L6
             62 S L5 AND DOMAIN?
L7
             24 DUP REM L6 (38 DUPLICATES REMOVED)
          39787 S IMMUNOGLOBULIN? AND (PROTEIN L OR LIGHT CHAIN OR
L8
HYBRID)
           9085 S L8 AND DOMAIN?
L9
L10
            850 S L9 AND IMMUNOGLOBULIN G
L11
             42 S L10 AND PROTEIN L
             31 DUP REM L11 (11 DUPLICATES REMOVED)
L12
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=> s 110 and hybrid protein

L13 143 L10 AND HYBRID PROTEIN

=> dup rem 113

PROCESSING COMPLETED FOR L13

L14 130 DUP REM L13 (13 DUPLICATES REMOVED)

=> d bib 100-130

L14 ANSWER 100 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AN 95006043 EMBASE

DN 1995006043

TI Baculovirus-insect cell production of bioactive choriogonadotropin-

immunoglobulin G heavy-chain fusion proteins in sheep.

AU Johnson G.A.; Hansen T.R.; Austin K.J.; Van Kirk E.A.; Murdoch W.J.

CS Department of Animal Science, University of Wyoming, Laramie, WY 82071,

```
United States
     Biology of Reproduction, (1995) 52/1 (68-73).
SO
     ISSN: 0006-3363 CODEN: BIREBV
     United States
CY
DT
     Journal; Article
FS
     003
             Endocrinology
             Immunology, Serology and Transplantation
     026
     English
LΑ
SL
    English
    ANSWER 101 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
L14
ΑN
     94366689 EMBASE
DN
    1994366689
ΤI
    Regulation of p68 RNA helicase by calmodulin and protein kinase
C.
ΑU
     Buelt M.K.; Glidden B.J.; Storm D.R.
CS
     Department of Pharmacology, University of Washington, Seattle, WA
98195,
     United States
SO
     Journal of Biological Chemistry, (1994) 269/47 (29367-29370).
     ISSN: 0021-9258 CODEN: JBCHA3
CY
     United States
     Journal; Article
DT
             Clinical Biochemistry
FS
     029
     030
             Pharmacology
     037
            Drug Literature Index
LΑ
     English
SL
     English
L14 ANSWER 102 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN
     94306346 EMBASE
DN
     1994306346
     The disulfide linkages and glycosylation sites of the human
TI
natriuretic
     peptide receptor-C homodimer.
     Stults J.T.; O'Connell K.L.; Garcia C.; Wong S.; Engel A.M.;
AU
Garbers D.L.;
     Lowe D.G.
     Cardiovascular Research Department, Genentech, Inc., South San
CS
Francisco,
     CA 94080, United States
     Biochemistry, (1994) 33/37 (11372-11381).
SO
     ISSN: 0006-2960 CODEN: BICHAW
CY
     United States
     Journal; Article
DT
FS
             Clinical Biochemistry
     029
LA
     English
SL
     English
     ANSWER 103 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
L14
AN
     94186627 EMBASE
DN
     1994186627
     Expression and subcellular localization of poliovirus
VPg-precursor
     protein 3AB in eukaryotic cells: Evidence for glycosylation in
vitro.
     Datta U.; Dasqupta A.
     Microbiology/Immunology Department, Jonsson Comprehensive Cancer
CS
Center,
```

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University of California, Los Angeles, CA 90024-1747, United
States
     Journal of Virology, (1994) 68/7 (4468-4477).
SO
     ISSN: 0022-538X CODEN: JOVIAM
CY
     United States
DT
     Journal; Article
FS
     004
             Microbiology
LA
     English
SL
     English
L14 ANSWER 104 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN
     94299231 EMBASE
DN
     1994299231
ΤI
     Passive immunity to yersiniae mediated by anti-recombinant V
antigen and
     protein A-V antigen fusion peptide.
ΑU
     Motin V.L.; Nakajima R.; Smirnov G.B.; Brubaker R.R.
CS
     Department of Microbiology, Michigan State University, East
Lansing, MI
     48824, United States
SO
     Infection and Immunity, (1994) 62/10 (4192-4201).
     ISSN: 0019-9567 CODEN: INFIBR
CY
     United States
DT
     Journal; Article
            Microbiology
FS
     004
     026
             Immunology, Serology and Transplantation
     037
             Drug Literature Index
LΑ
     English
SL
     English
L14 ANSWER 105 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN
     94105139 EMBASE
DN
     1994105139
     Mechanism of lymphocyte function-associated molecule 3-Ig fusion
ΤI
proteins
     inhibition of T cell responses: Structure/function analysis in
vitro and
     in human CD2 transgenic mice.
     Majeau G.R.; Meier W.; Jimmo B.; Kioussis D.; Hochman P.S.
ΑU
CS
     Biogen, Inc., 14 Cambridge Center, Cambridge, MA 02142, United
States
     Journal of Immunology, (1994) 152/6 (2753-2767).
SO
     ISSN: 0022-1767 CODEN: JOIMA3
CY
     United States
DT
     Journal; Article
FS
             Immunology, Serology and Transplantation
     026
     029
             Clinical Biochemistry
     037
            Drug Literature Index
LA
    English
    English
SL
    ANSWER 106 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
L14
AN
     94091699 EMBASE
DN
     1994091699
ΤI
    Characterization of domains of herpes simplex virus type 1
     glycoprotein E involved in Fc binding activity for immunoglobulin
     G aggregates.
    Dubin G.; Basu S.; Mallory D.L.P.; Basu M.; Tal-Singer R.;
Friedman H.M.
```

```
Infectious Diseases Division, 536 Johnson Pavilion, University of
CS
     Pennsylvania, Philadelphia, PA 19104-6073, United States
SO
     Journal of Virology, (1994) 68/4 (2478-2486).
     ISSN: 0022-538X CODEN: JOVIAM
CY
     United States
DT
     Journal; Article
FS
     004
             Microbiology
             Immunology, Serology and Transplantation
     026
LA
     English
\mathtt{SL}
     English
L14 ANSWER 107 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
     94362409 EMBASE
AN
DN
     1994362409
TI
     Recombinant thyrotropin receptor and the induction of autoimmune
thyroid
     disease in BALB/c mice: A new animal model.
     Costagliola S.; Many M.C.; Stalmans-Falys M.; Tonacchera M.;
Vassart G.;
     Ludgate M.
CS
     IRIBHN, Universite Libre de Bruxelles, Campus Hopital Erasme,
808 route de
     Lennik, B-1070 Brussel, Belgium
SO
     Endocrinology, (1994) 135/5 (2150-2159).
     ISSN: 0013-7227 CODEN: ENDOAO
CY
     United States
\mathtt{DT}
    Journal; Article
FS
     003
             Endocrinology
     026
             Immunology, Serology and Transplantation
     037
             Drug Literature Index
     English
LΑ
\operatorname{SL}
     English
L14 ANSWER 108 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ΑN
     94273456 EMBASE
DN
     1994273456
TI
     Expression of a fibrinolytically active human pro-urokinase
fusion protein
     in Escherichia coli.
ΑU
     Hua Z.; Jie L.; Zhu D.
CS
     Department of Biochemistry, Nanjing University, Nanjing 210008,
China
     Biochemistry and Molecular Biology International, (1994) 33/6
SO
(1215-1220).
     ISSN: 1039-9712 CODEN: BMBIES
CY
     Australia
DT
     Journal; Article
FS
     029
             Clinical Biochemistry
LA
     English
\operatorname{SL}
     English
L14 ANSWER 109 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN
     94160331 EMBASE
DN
     1994160331
TI
     A single Fc binding domain-alkaline phosphatase gene fusion
     expresses a protein with both IgG binding ability and alkaline
phosphatase
     enzymatic activity.
ΑU
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       Chiron Corporation, Emeryville, CA, United States (U.S.
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RLI
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      now abandoned which is a continuation-in-part of Ser. No. US
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       continuation-in-part of Ser. No. US 1984-667501, filed on 31
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      now abandoned
DT
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FS
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EXNAM Primary Examiner: Nucker, Christine M.; Assistant Examiner:
Woodward, M.
      Ρ.
LREP
      Blackburn, Robert P., McClung, Barbara G., Shetka, Debra A.
CLMN
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      Exemplary Claim: 1
DRWN
       61 Drawing Figure(s); 59 Drawing Page(s)
LN.CNT 4178
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L14
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       92:72398 USPATFULL
TI
       Construction of an IgG binding protein to facilitate downstream
      processing using protein engineering
IN
       Abrahmsen, Lars, Stockholm, Sweden
      Moks, Tomas, Taby, Sweden
      Nilsson, Bjorn, Sollentuna, Sweden
      Uhlen, Mathias, Upsala, Sweden
       KabiGen AB, Stockholm, Sweden (non-U.S. corporation)
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EXNAM Primary Examiner: Lacey, David L.; Assistant Examiner: Ulm,
John D.
      Burns, Doane, Swecker, & Mathis
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      Exemplary Claim: 1
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    ANSWER 120 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
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     029
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L14 ANSWER 121 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
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L14 ANSWER 122 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
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     029
             Clinical Biochemistry
     037
             Drug Literature Index
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     026
             Immunology, Serology and Transplantation
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     037
            Drug Literature Index
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     1991:317905 BIOSIS
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SUBUNITS FROM RHODOBACTER-SPHAEROIDES WILD-TYPE PROTEINS AND **FUSION** PROTEINS CONTAINING ONE OR FOUR TRUNCATED DOMAINS FROM STAPHYLOCOCCUS-AUREUS PROTEIN A AT THE CARBOXY-TERMINUS. ΑU SOEHLEMANN P; OECKL C; MICHEL H LABORATORIUM MOLEKULARE BIOLOGIE, GENZENTRUM, AM KLOPFERSPITZ CS 18A, D-8033 MARTINSRIED, W. GER. BIOCHIM BIOPHYS ACTA, (1991) 1089 (1), 103-112. SO CODEN: BBACAQ. ISSN: 0006-3002. FS BA; OLD LΑ English L14 ANSWER 130 OF 130 BIOSIS COPYRIGHT 2002 BIOSIS DUPLICATE 7 AN 1990:235460 BIOSIS DN BA89:122413 AFFINITY IMMOBILIZATION OF A GENETICALLY ENGINEERED BIFUNCTIONAL ΤI HYBRID PROTEIN. ΑU BANEYX F; SCHMIDT C; GEORGIOU G DEP. CHEMICAL ENGINEERING, UNIV. TEXAS AT AUSTIN, AUSTIN, TEX. CS 78712. ENZYME MICROB TECHNOL, (1990) 12 (5), 337-342. SO CODEN: EMTED2. ISSN: 0141-0229. FS BA; OLD LΑ English => d bib 100-130 L14 ANSWER 100 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V. AN95006043 EMBASE DN 1995006043 Baculovirus-insect cell production of bioactive TIchoriogonadotropinimmunoglobulin G heavy-chain fusion proteins in sheep. ΑU Johnson G.A.; Hansen T.R.; Austin K.J.; Van Kirk E.A.; Murdoch W.J. Department of Animal Science, University of Wyoming, Laramie, WY CS 82071, United States Biology of Reproduction, (1995) 52/1 (68-73). SO ISSN: 0006-3363 CODEN: BIREBV CY United States DTJournal: Article FS 003 Endocrinology 026 Immunology, Serology and Transplantation LA English SL English ANSWER 101 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V. L14AN 94366689 EMBASE 1994366689 DNTIRegulation of p68 RNA helicase by calmodulin and protein kinase C. ΑU Buelt M.K.; Glidden B.J.; Storm D.R. CS Department of Pharmacology, University of Washington, Seattle, WA

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     037
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     English
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L14 ANSWER 105 OF 130
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     94105139 EMBASE
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    Mechanism of lymphocyte function-associated molecule 3-Ig fusion
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             Drug Literature Index
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LA
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    ANSWER 106 OF 130 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
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AN
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phosphatase
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ID 83844,
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L14
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AN
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ΤI
     Gene synthesis and functional expression of a protein exhibiting
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L4
            233 S L3 AND IMMUNOGLOBULIN?
L5
            102 S L4 AND (PROTEIN L OR LIGHT CHAIN OR HYBRID)
L6
            62 S L5 AND DOMAIN?
L7
            24 DUP REM L6 (38 DUPLICATES REMOVED)
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L8 HYBRID)	39787	S IMMUNOGLOBULIN? AND (PROTEIN L OR LIGHT CHAIN OR
L9	9085	S L8 AND DOMAIN?
L10	850	S L9 AND IMMUNOGLOBULIN G
L11	42	S L10 AND PROTEIN L
L12	31	DUP REM L11 (11 DUPLICATES REMOVED)
L13	143	S L10 AND HYBRID PROTEIN
L14	130	DUP REM L13 (13 DUPLICATES REMOVED)

=> s l14 and domain?

L15 130 L14 AND DOMAIN?